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09/704,306

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(FILE 'HOME' ENTERED AT 11:03:59 ON 14 MAR 2003)

FILE 'REGISTRY' ENTERED AT 11:04:03 ON 14 MAR 2003

L1 STRUCTURE UPLOADED

L2 QUE L1

L3 28 S L2

L4 1187 S L2 SSS FUL

FILE 'CAPLUS' ENTERED AT 11:06:02 ON 14 MAR 2003

L5 1149 S L4

FILE 'REGISTRY' ENTERED AT 11:07:16 ON 14 MAR 2003

L6 STRUCTURE UPLOADED

L7 QUE L6

L8 45 S L7 SUB=L4 SAM

L9 STRUCTURE UPLOADED

L10 QUE L9

~~L11 26 S L10 SUB=L4 SAM~~

L12 986 S L7 SUB=L4 FUL

L13 686 S L10 SUB=L4 FUL

L14 STRUCTURE UPLOADED

L15 QUE L14

L16 771 S L15 SUB=L4 FUL

FILE 'CAPLUS' ENTERED AT 11:12:31 ON 14 MAR 2003

L17 1092 S L16

L18 ANALYZE L17 1- RN HIT : 756 TERMS

FILE 'REGISTRY' ENTERED AT 11:13:58 ON 14 MAR 2003

L19 1 S 24526-64-5/RN

L20 1 S 32795-47-4/RN

L21 769 S L16 NOT (L19 OR L20)

FILE 'CAPLUS' ENTERED AT 11:16:57 ON 14 MAR 2003

L22 225 S L21

FILE 'REGISTRY' ENTERED AT 11:19:20 ON 14 MAR 2003

L23 STRUCTURE UPLOADED

L24 QUE L23

L25 299 S L24 SUB=L4 FUL

L26 472 S L16 NOT L25

FILE 'CAPLUS' ENTERED AT 11:21:00 ON 14 MAR 2003

L27 142 S L26

L28 ANALYZE L27 1- RN HIT : 471 TERMS

FILE 'REGISTRY' ENTERED AT 11:21:42 ON 14 MAR 2003

FILE 'REGISTRY' ENTERED AT 11:21:49 ON 14 MAR 2003

FILE 'CAPLUS' ENTERED AT 11:22:34 ON 14 MAR 2003

L29 21 S L27 AND PATENT/DT

L30 121 S L27 NOT L29

L31 0 S L30 AND 2003/SO

L32 5 S L30 AND 2002/SO

L33 5 S L30 AND 2001/SO

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L34 4 S L30 AND 2000/SO  
L35 129 S L27 NOT (L32 OR L33 OR L34)

FILE 'REGISTRY' ENTERED AT 11:24:38 ON 14 MAR 2003  
L36 STRUCTURE UPLOADED  
L37 QUE L36  
L38 771 S L37 SUB=L4 FUL

FILE 'CAPLUS' ENTERED AT 11:25:52 ON 14 MAR 2003  
L39 108 S L30 NOT (L32 OR L33 OR L34)  
L40 ANALYZE L39 1- RN HIT : 146 TERMS

FILE 'REGISTRY' ENTERED AT 11:26:55 ON 14 MAR 2003  
L41 1 S 67165-56-4/RN  
L42 1 S 26996-80-5/RN  
L43 1 S 23367-61-5/RN

FILE 'CAPLUS' ENTERED AT 11:28:16 ON 14 MAR 2003  
L44 18 S L42  
L45 20 S L43  
L46 38 S L44 OR L45  
L47 79 S L39 NOT L46

FILE 'REGISTRY' ENTERED AT 11:31:21 ON 14 MAR 2003

FILE 'CAPLUS' ENTERED AT 11:32:03 ON 14 MAR 2003  
L48 100 S L29 OR L47

=> d bib abs hitstr 1-100

09/704,306

L48 ANSWER 1 OF 100 CAPLUS COPYRIGHT 2003 ACS

AN 2001:488632 CAPLUS

DN 135:92550

TI Preparation of tetrahydroisoquinolines as estrogen agonists/antagonists

IN Chesworth, Richard; Cameron, Kimberly O'Keefe; Da Silva-Jardine, Paul  
Andrew; Day, Robert Francis; Lefker, Bruce Allen; Zawistoski, Michael Paul

PA Pfizer Inc., USA

SO Eur. Pat. Appl., 66 pp.

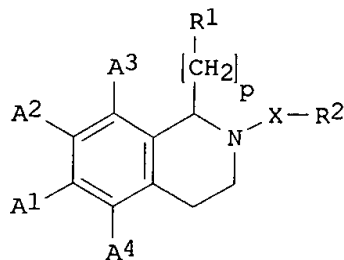
CODEN: EPXXDW

DT Patent

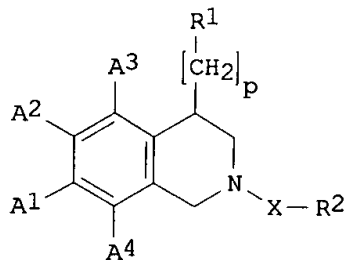
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1113007	A1	20010704	EP 2000-311197	20001214
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	US 2001039285	A1	20011108	US 2000-745396	20001221
	JP 2001294575	A2	20011023	JP 2000-389883	20001222
	BR 2000006265	A	20020305	BR 2000-6265	20001222
PRAI	US 1999-173063P	P	19991224		
OS	MARPAT 135:92550				
GI					



I



II

AB The title compds. [I; A1 = H, OH, alkoxy, etc.; A2-A4 = H, OH, alkoxy, halo; R1 = (un)substituted Ph, pyridyl, piperidiny, etc.; X = a bond, (CH2)<sub>n</sub> (n = 1-3), CO2, etc.; R2 = alkyl, alkenyl, benzhydryl, etc.; p = 0-2], useful for treating or preventing obesity, breast cancer, osteoporosis, endometriosis, cardiovascular disease, prostatic disease, and the like, were prepd. Thus, hydrogenation of 1-[1-(4-benzoyloxyphenyl)-6-methoxy-3,4-dihydro-1H-isoquinolin-2-yl]-2,2,2-trifluoroethanone over 10% Pd/C in EtOH afforded 88% I [A1 = OMe; A2-A4 = H; R1 = 4-HOC6H4; p = 0; X = CO; R2 = CF3].

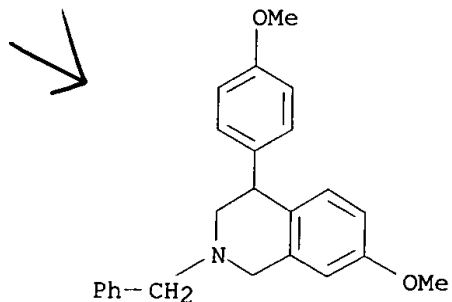
IT 347977-80-4P 347982-87-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

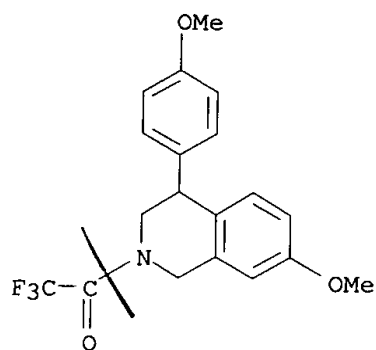
(prepn. of tetrahydroisoquinolines as estrogen agonists/antagonists)

RN 347977-80-4 CAPLUS

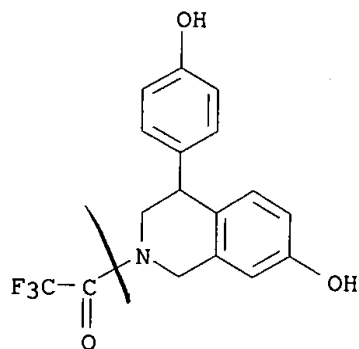
CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-4-(4-methoxyphenyl)-2-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 347982-87-0 CAPLUS  
 CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-4-(4-methoxyphenyl)-2-(trifluoroacetyl)- (9CI) (CA INDEX NAME)



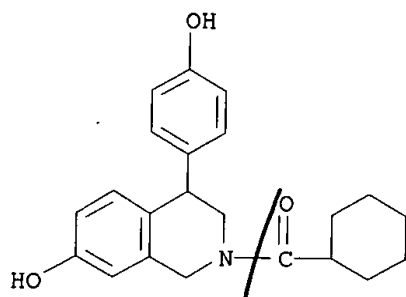
IT **347982-93-8P 347982-98-3P 347983-02-2P**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of tetrahydroisoquinolines as estrogen agonists/antagonists)  
 RN 347982-93-8 CAPLUS  
 CN 7-Isoquinolinol, 1,2,3,4-tetrahydro-4-(4-hydroxyphenyl)-2-(trifluoroacetyl)- (9CI) (CA INDEX NAME)



RN 347982-98-3 CAPLUS

09/704,306

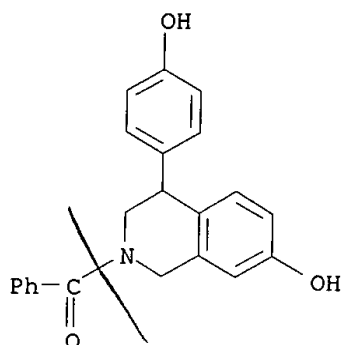
CN 7-Isoquinolinol, 2-(cyclohexylcarbonyl)-1,2,3,4-tetrahydro-4-(4-hydroxyphenyl)- (9CI) (CA INDEX NAME)



RN 347983-02-2 CAPLUS

CN 7-Isoquinolinol, 2-benzoyl-1,2,3,4-tetrahydro-4-(4-hydroxyphenyl)- (9CI)  
(CA INDEX NAME)

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RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

09/704,306

ANSWER 2 OF 100 CAPLUS COPYRIGHT 2003 ACS

AN 2001:338496 CAPLUS

DN 134:353258

TI Aryl- and heteroaryl-substituted tetrahydroisoquinolines and use thereof to block reuptake of norepinephrine, dopamine and serotonin

IN Beck, James P.; Curry, Matt A.; Smith, Mark A.

PA Du Pont Pharmaceuticals Company, USA

SO PCT Int. Appl., 66 pp.

CODEN: PIXXD2

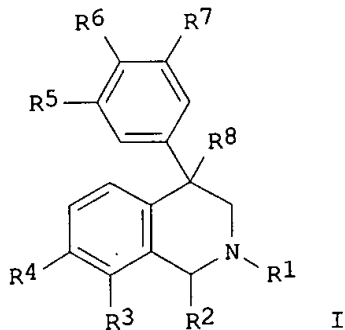
DT **Patent**

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001032625	A1	20010510	WO 2000-US30329	20001103
	W: AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
	BR 2000015320	A	20020709	BR 2000-15320	20001103
	EP 1246806	A1	20021009	EP 2000-976885	20001103
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR				
	US 2002143014	A1	20021003	US 2002-91949	20020306
PRAI	US 1999-163269P	P	<u>19991103</u>		
	US 2000-704305	B1	20001102		
	WO 2000-US30329	W	20001103		
OS	MARPAT 134:353258				
GI					

not  
prior  
art  
no  
odp



AB Diarylmethyltetrahydroisoquinolines (4R)- or (4S)-I [R1 = (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl; R2 = H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, haloalkyl; R3 = H, halogen, (un)substituted OH, S(O)nH, CN, CHO, CONH2, alkyl, alkenyl, alkynyl, cycloalkyl; R4 = (un)substituted aryl, heteroaryl; R5-R7 = H, halogen, CN, (un)substituted OH, NH2, S(O)nH, CHO, CONH2, alkyl, alkenyl, alkynyl, cycloalkyl; R8 = H, (un)substituted OH; n = 0-2] were prepd. for use as blockers of the reuptake of norepinephrine, dopamine and serotonin (no data). Thus, 3-bromobenzaldehyde is stirred in the presence of methylamine and reduced

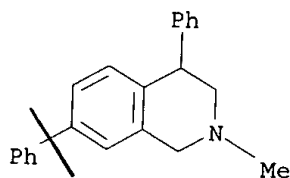
with sodium borohydride followed by addn. of .alpha.-chloroacetophenone and redn. of the amino ketone in situ with sodium borohydride to give 3-BrC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>N(Me)CH<sub>2</sub>CH(OH)Ph; cyclization of the benzyl alc. with sulfuric acid followed by coupling with phenylboronic acid gave I (R<sub>1</sub> = Me; R<sub>4</sub> = Ph; R<sub>2</sub> = R<sub>3</sub> = R<sub>5</sub> = R<sub>6</sub> = R<sub>7</sub> = H) as an oil. Such compds. are particularly useful in the treatment of a neurol. and psychiatric disorders which are created by or are dependent upon decreased availability of serotonin, norepinephrine or dopamine, such as attention deficit-hyperactivity disorder (ADHD), anxiety, depression, and addiction disorders.

IT 338997-50-5P 338997-52-7P 338997-54-9P  
 338997-56-1P 338997-58-3P 338997-60-7P  
 338997-62-9P 338997-64-1P 338998-03-1P  
 338998-05-3P 338998-07-5P 338998-09-7P  
 338998-11-1P 338998-13-3P 338998-15-5P  
 338998-17-7P 338998-52-0P 338998-54-2P  
 338998-56-4P 338998-58-6P 338998-59-7P  
 338998-60-0P 338998-61-1P 338998-62-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of diarylmethyltetrahydroisoquinolines as selective reuptake inhibitors of dopamine, norepinephrine, and serotonin)

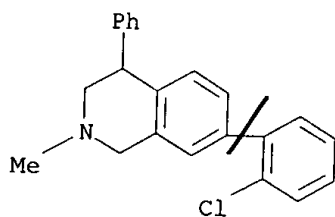
RN 338997-50-5 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-2-methyl-4,7-diphenyl- (9CI) (CA INDEX NAME)



RN 338997-52-7 CAPLUS

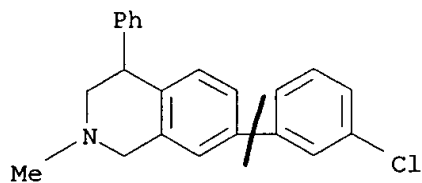
CN Isoquinoline, 7-(2-chlorophenyl)-1,2,3,4-tetrahydro-2-methyl-4-phenyl- (9CI) (CA INDEX NAME)



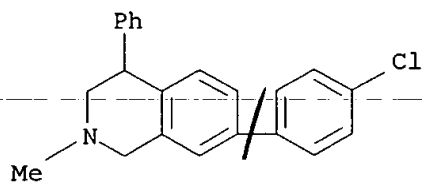
RN 338997-54-9 CAPLUS

CN Isoquinoline, 7-(3-chlorophenyl)-1,2,3,4-tetrahydro-2-methyl-4-phenyl- (9CI) (CA INDEX NAME)

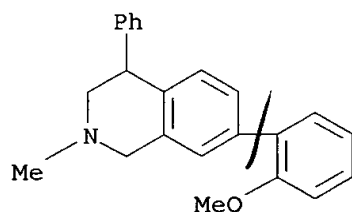




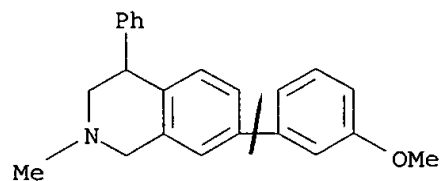
RN 338997-56-1 CAPLUS  
CN Isoquinoline, 7-(4-chlorophenyl)-1,2,3,4-tetrahydro-2-methyl-4-phenyl-  
(9CI) (CA INDEX NAME)



RN 338997-58-3 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-7-(2-methoxyphenyl)-2-methyl-4-phenyl-  
(9CI) (CA INDEX NAME)

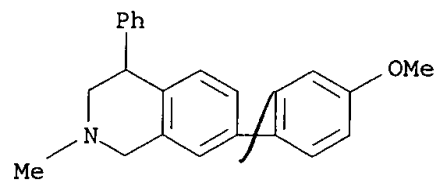


RN 338997-60-7 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-7-(3-methoxyphenyl)-2-methyl-4-phenyl-  
(9CI) (CA INDEX NAME)



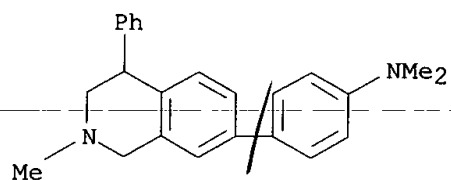
RN 338997-62-9 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-7-(4-methoxyphenyl)-2-methyl-4-phenyl-  
(9CI) (CA INDEX NAME)

09/704,306



RN 338997-64-1 CAPLUS

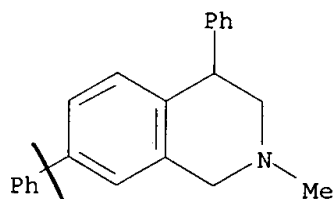
CN Benzenamine, N,N-dimethyl-4-(1,2,3,4-tetrahydro-2-methyl-4-phenyl-7-isoquinolinyl)- (9CI) (CA INDEX NAME)



RN 338998-03-1 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-2-methyl-4,7-diphenyl-, (+)- (9CI) (CA INDEX NAME)

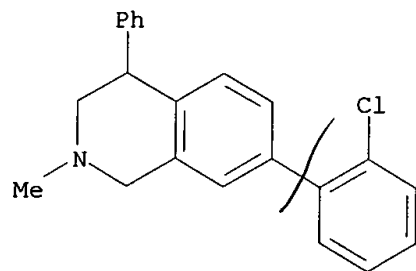
Rotation (+).



RN 338998-05-3 CAPLUS

CN Isoquinoline, 7-(2-chlorophenyl)-1,2,3,4-tetrahydro-2-methyl-4-phenyl-, (+)- (9CI) (CA INDEX NAME)

Rotation (+).

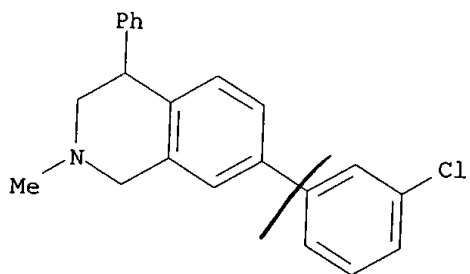


RN 338998-07-5 CAPLUS

CN Isoquinoline, 7-(3-chlorophenyl)-1,2,3,4-tetrahydro-2-methyl-4-phenyl-, (+)- (9CI) (CA INDEX NAME)

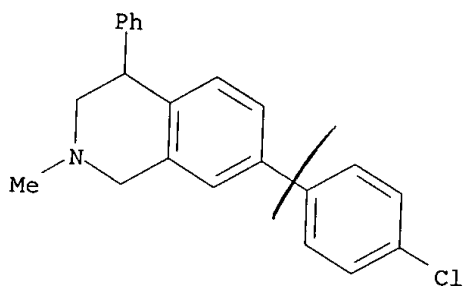
09/704,306

Rotation (+).



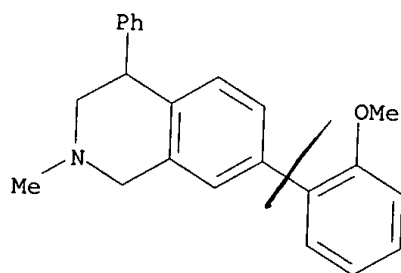
RN 338998-09-7 CAPLUS  
CN Isoquinoline, 7-(4-chlorophenyl)-1,2,3,4-tetrahydro-2-methyl-4-phenyl-,  
(+)- (9CI) (CA INDEX NAME)

Rotation (+).



RN 338998-11-1 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-7-(2-methoxyphenyl)-2-methyl-4-phenyl-,  
(+)- (9CI) (CA INDEX NAME)

Rotation (+).



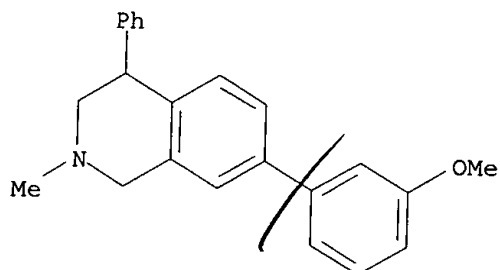
RN 338998-13-3 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-7-(3-methoxyphenyl)-2-methyl-4-phenyl-,  
(+)- (9CI) (CA INDEX NAME)

Rotation (+).

Brenda Coleman

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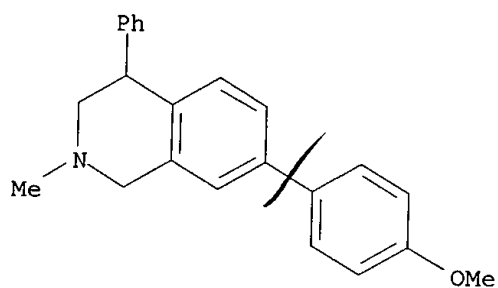
09/704,306



RN 338998-15-5 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-7-(4-methoxyphenyl)-2-methyl-4-phenyl-,  
(+)- (9CI) (CA INDEX NAME)

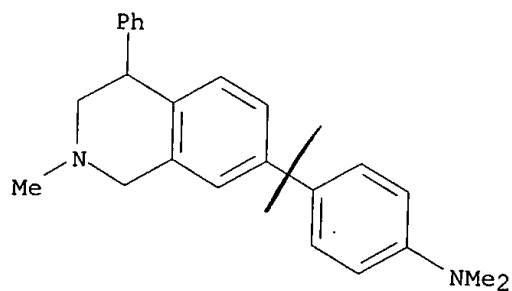
Rotation (+).



RN 338998-17-7 CAPLUS

CN Benzenamine, N,N-dimethyl-4-(1,2,3,4-tetrahydro-2-methyl-4-phenyl-7-  
isoquinolinyl)-, (+)- (9CI) (CA INDEX NAME)

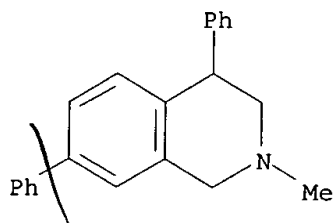
Rotation (+).



RN 338998-52-0 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-2-methyl-4,7-diphenyl-, (-)- (9CI) (CA  
INDEX NAME)

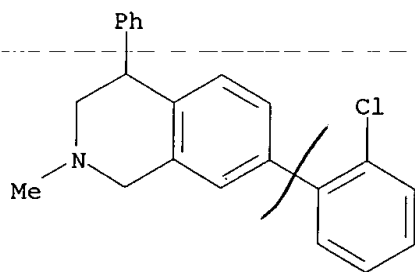
Rotation (-).



RN 338998-54-2 CAPLUS

CN Isoquinoline, 7-(2-chlorophenyl)-1,2,3,4-tetrahydro-2-methyl-4-phenyl-,  
(-)- (9CI) (CA INDEX NAME)

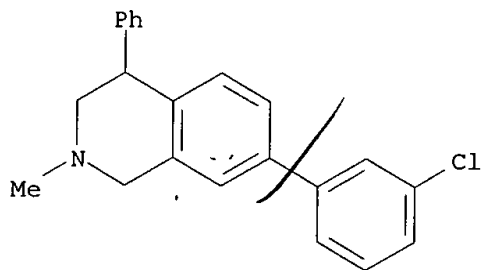
Rotation (-).



RN 338998-56-4 CAPLUS

CN Isoquinoline, 7-(3-chlorophenyl)-1,2,3,4-tetrahydro-2-methyl-4-phenyl-,  
(-)- (9CI) (CA INDEX NAME)

Rotation (-).

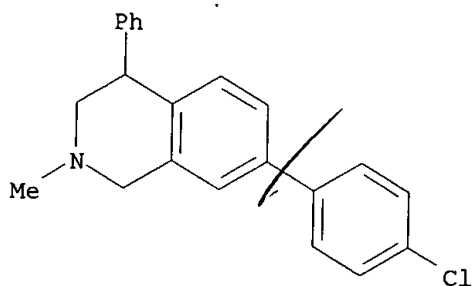


RN 338998-58-6 CAPLUS

CN Isoquinoline, 7-(4-chlorophenyl)-1,2,3,4-tetrahydro-2-methyl-4-phenyl-,  
(-)- (9CI) (CA INDEX NAME)

Rotation (-).

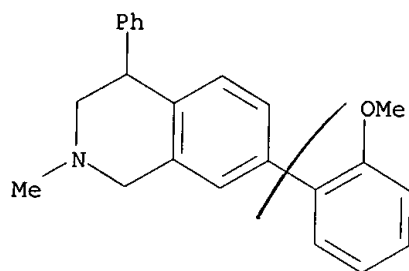
09/704,306



RN 338998-59-7 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-7-(2-methoxyphenyl)-2-methyl-4-phenyl-,  
(-)- (9CI) (CA INDEX NAME)

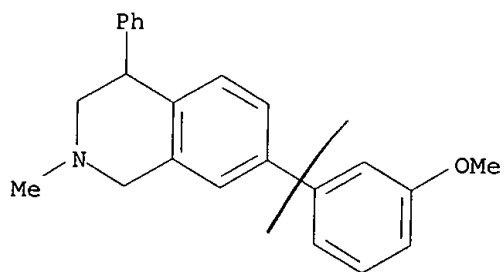
Rotation (-).

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RN 338998-60-0 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-7-(3-methoxyphenyl)-2-methyl-4-phenyl-,  
(-)- (9CI) (CA INDEX NAME)

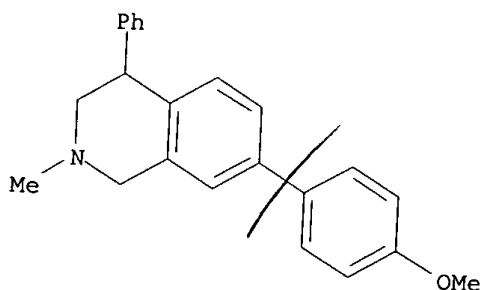
Rotation (-).



RN 338998-61-1 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-7-(4-methoxyphenyl)-2-methyl-4-phenyl-,  
(-)- (9CI) (CA INDEX NAME)

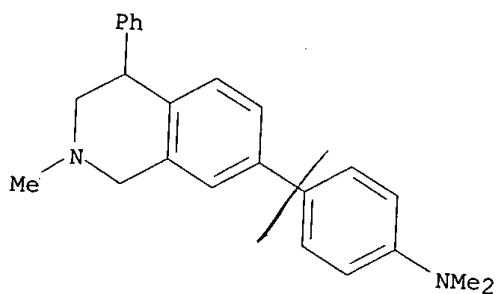
Rotation (-).

09/704,306



RN 338998-62-2 CAPLUS  
CN Benzenamine, N,N-dimethyl-4-(1,2,3,4-tetrahydro-2-methyl-4-phenyl-7-isoquinolinyl)-, (-)- (9CI) (CA INDEX NAME)

Rotation (-).

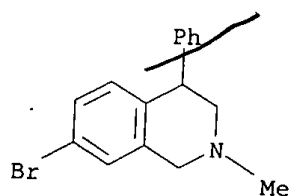


IT 338998-82-6P 338998-87-1P 338998-89-3P  
338998-92-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. of diarylmethyltetrahydroisoquinolines as selective reuptake inhibitors of dopamine, norepinephrine, and serotonin)

RN 338998-82-6 CAPLUS

CN Isoquinoline, 7-bromo-1,2,3,4-tetrahydro-2-methyl-4-phenyl- (9CI) (CA INDEX NAME)

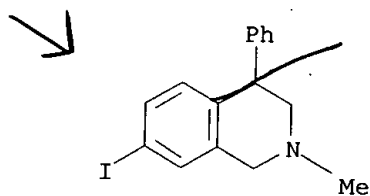


RN 338998-87-1 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-7-iodo-2-methyl-4-phenyl- (9CI) (CA INDEX NAME)

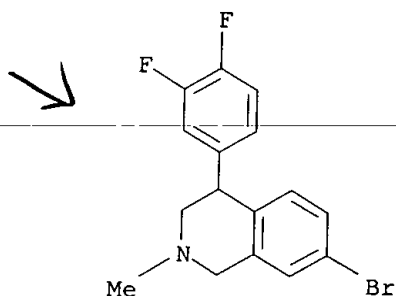
Brenda Coleman

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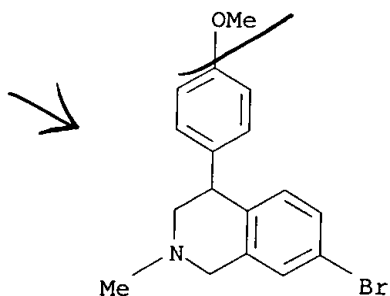
RN 338998-89-3 CAPLUS

CN Isoquinoline, 7-bromo-4-(3,4-difluorophenyl)-1,2,3,4-tetrahydro-2-methyl-  
(9CI) (CA INDEX NAME)



RN 338998-92-8 CAPLUS

CN Isoquinoline, 7-bromo-1,2,3,4-tetrahydro-4-(4-methoxyphenyl)-2-methyl-  
(9CI) (CA INDEX NAME)



IT **338998-83-7P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of diarylmethyltetrahydroisoquinolines as selective reuptake  
inhibitors of dopamine, norepinephrine, and serotonin)

RN 338998-83-7 CAPLUS

CN Isoquinoline, 7-bromo-1,2,3,4-tetrahydro-2-methyl-4-phenyl-,  
(2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

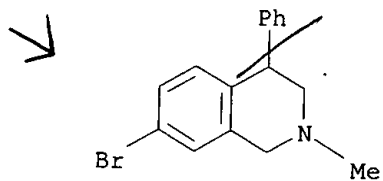
CM 1

CRN 338998-82-6

CMF C16 H16 Br N



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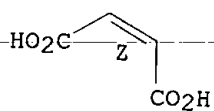


CM 2

CRN 110-16-7

CMF C4 H4 O4

Double bond geometry as shown.



RE.CNT 8

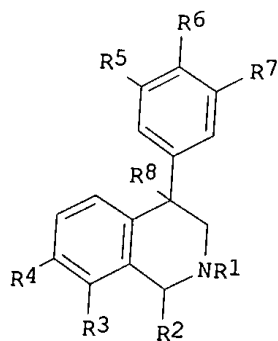
THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

09/704,306

applicant

L48 ANSWER 3 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 2001:338495 CAPLUS  
DN 134:353257  
TI 4-Phenyltetrahydroisoquinolines and use thereof to block reuptake of  
norepinephrine, dopamine and serotonin  
IN Beck, James P.; Smith, Mark A.  
PA Du Pont Pharmaceuticals Company, USA  
SO PCT Int. Appl., 79 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001032624	A1	20010510	WO 2000-US30328	20001103
W: AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
BR 2000015307	A	20020709	BR 2000-15307	20001103
EP 1246805	A1	20021009	EP 2000-976884	20001103
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR				
PRAI US 1999-163270P	P	19991103		
WO 2000-US30328	W	20001103		
OS MARPAT 134:353257				
GI				



AB Tetrahydroisoquinolines I [R1 = (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl; R2 = H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, haloalkyl; R3-R7 = H, halogen, (un)substituted OH, S(O)nH, S(O)nNH2, CN, acyl, CONH2, alkyl, alkenyl, alkynyl, cycloalkyl; R8 = H, halogen, (un)substituted OH] were prepd. for use as inhibitors of the uptake of norepinephrine, dopamine and serotonin in the treatment of various neurol. and psychiatric disorders, e.g. ADHD (no data). Thus, 3-MeC6H4CHO was reductively alkylated with HOCHPhCH2NHMe and cyclized with 98% H2SO4 to give 2,7-dimethyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline.

IT 339001-11-5P  
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)

Brenda Coleman

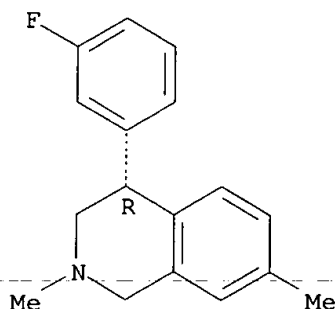
09/704,306

(prepn. of 4-phenyltetrahydroisoquinolines and use thereof to block reuptake of norepinephrine, dopamine and serotonin).

RN 339001-11-5 CAPLUS

CN Isoquinoline, 4-(3-fluorophenyl)-1,2,3,4-tetrahydro-2,7-dimethyl-, (4R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



C, E

IT 339000-96-3P 339000-98-5P 339001-04-6P

339001-06-8P 339001-08-0P

RL: PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of 4-phenyltetrahydroisoquinolines and use thereof to block reuptake of norepinephrine, dopamine and serotonin)

RN 339000-96-3 CAPLUS

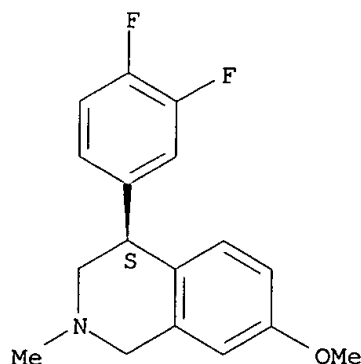
CN Isoquinoline, 4-(3,4-difluorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-, (4S)-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 339000-95-2

CMF C17 H17 F2 N O

Absolute stereochemistry. Rotation (+).



C, E

CM 2

CRN 110-16-7

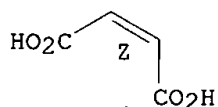
Brenda Coleman

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09/704,306

CMF C4 H4 O4

Double bond geometry as shown.



RN 339000-98-5 CAPLUS

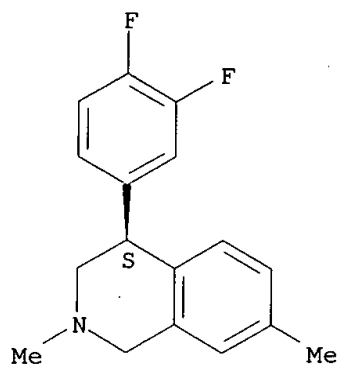
CN Isoquinoline, 4-(3,4-difluorophenyl)-1,2,3,4-tetrahydro-2,7-dimethyl-,  
(4S)-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 339000-97-4

CMF C17 H17 F2 N

Absolute stereochemistry. Rotation (+).



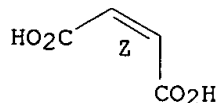
C, E

CM 2

CRN 110-16-7

CMF C4 H4 O4

Double bond geometry as shown.



RN 339001-04-6 CAPLUS

CN Isoquinoline, 4-(3,5-difluorophenyl)-1,2,3,4-tetrahydro-2,7-dimethyl-,  
(4S)-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 339001-03-5

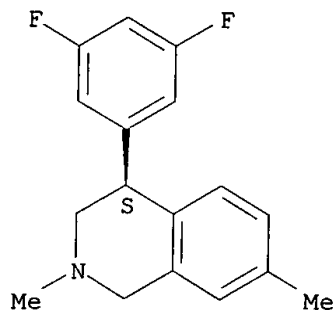
CMF C17 H17 F2 N

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Absolute stereochemistry. Rotation (+).

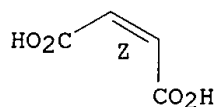


C,E

CM 2

CRN 110-16-7  
CMF C4 H4 O4

Double bond geometry as shown.

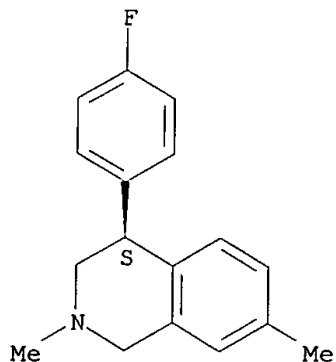


RN 339001-06-8 CAPLUS  
CN Isoquinoline, 4-(4-fluorophenyl)-1,2,3,4-tetrahydro-2,7-dimethyl-, (4S)-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 339001-05-7  
CMF C17 H18 F N

Absolute stereochemistry. Rotation (+).



C

CM 2

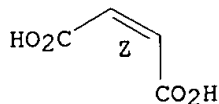
Brenda Coleman

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CRN 110-16-7  
CMF C4 H4 O4

Double bond geometry as shown.

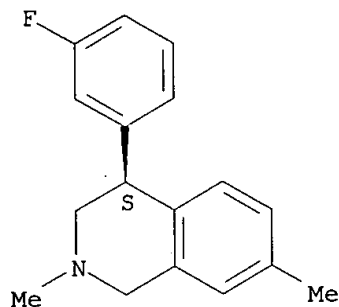


RN 339001-08-0 CAPLUS  
CN Isoquinoline, 4-(3-fluorophenyl)-1,2,3,4-tetrahydro-2,7-dimethyl-, (4S)-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 339001-07-9  
CMF C17 H18 F N

Absolute stereochemistry. Rotation (+).

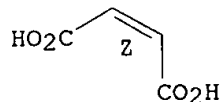


C, E

CM 2

CRN 110-16-7  
CMF C4 H4 O4

Double bond geometry as shown.



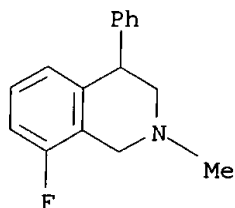
IT 129010-56-6P 129010-60-2P 339000-37-2P  
339001-31-9P 339001-32-0P 339001-35-3P  
339001-36-4P 339001-37-5P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(prepn. of 4-phenyltetrahydroisoquinolines and use thereof to block  
reuptake of norepinephrine, dopamine and serotonin)  
RN 129010-56-6 CAPLUS

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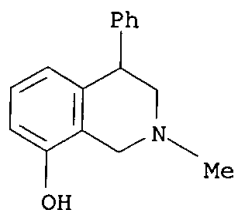
CN Isoquinoline, 8-fluoro-1,2,3,4-tetrahydro-2-methyl-4-phenyl- (9CI) (CA INDEX NAME)



*excluded*

RN 129010-60-2 CAPLUS

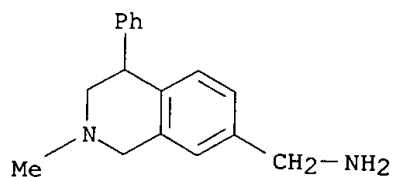
CN 8-Isoquinolinol, 1,2,3,4-tetrahydro-2-methyl-4-phenyl- (9CI) (CA INDEX NAME)



*exc.*

RN 339000-37-2 CAPLUS

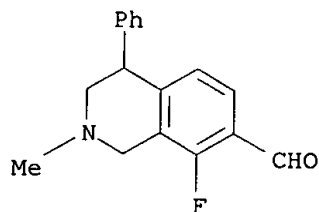
CN 7-Isoquinolinemethanamine, 1,2,3,4-tetrahydro-2-methyl-4-phenyl- (9CI) (CA INDEX NAME)



*C*

RN 339001-31-9 CAPLUS

CN 7-Isoquinolinecarboxaldehyde, 8-fluoro-1,2,3,4-tetrahydro-2-methyl-4-phenyl- (9CI) (CA INDEX NAME)



*exc.*

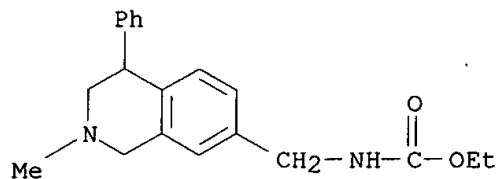
RN 339001-32-0 CAPLUS

Brenda Coleman

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09/704,306

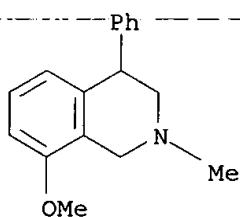
CN Carbamic acid, [(1,2,3,4-tetrahydro-2-methyl-4-phenyl-7-isoquinolinyl)methyl]-, ethyl ester (9CI) (CA INDEX NAME)



*exc.*

RN 339001-35-3 CAPLUS

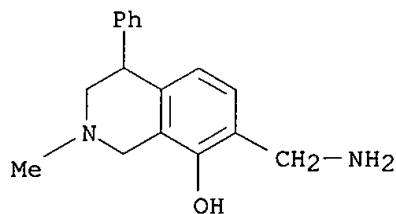
CN Isoquinoline, 1,2,3,4-tetrahydro-8-methoxy-2-methyl-4-phenyl- (9CI) (CA INDEX NAME)



*exc.*

RN 339001-36-4 CAPLUS

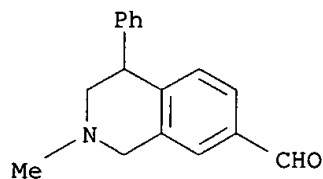
CN 8-Isoquinolinol, 7-(aminomethyl)-1,2,3,4-tetrahydro-2-methyl-4-phenyl- (9CI) (CA INDEX NAME)



*C*

RN 339001-37-5 CAPLUS

CN 7-Isoquinolinecarboxaldehyde, 1,2,3,4-tetrahydro-2-methyl-4-phenyl- (9CI) (CA INDEX NAME)



*exc.*

IT 338999-25-0P 338999-26-1P 338999-27-2P  
338999-28-3P 338999-29-4P 338999-30-7P  
338999-31-8P 338999-32-9P 338999-33-0P



338999-34-1P 338999-35-2P 338999-36-3P  
 338999-37-4P 338999-38-5P 338999-39-6P  
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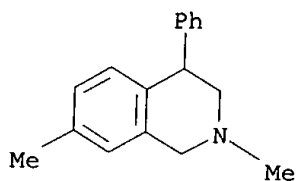
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of 4-phenyltetrahydroisoquinolines and use thereof to block reuptake of norepinephrine, dopamine and serotonin)

RN 338999-25-0 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-2,7-dimethyl-4-phenyl-, hydrochloride (9CI) (CA INDEX NAME)

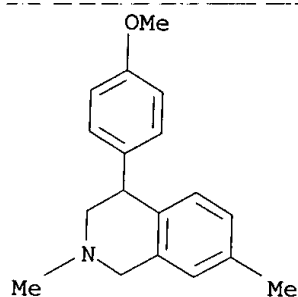
09/704,306



C

● HCl

RN 338999-26-1 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-4-(4-methoxyphenyl)-2,7-dimethyl- (9CI)  
(CA INDEX NAME)

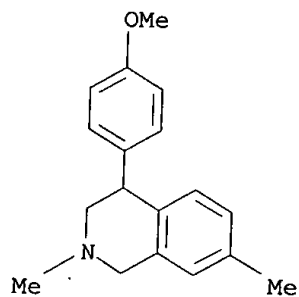


C

RN 338999-27-2 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-4-(4-methoxyphenyl)-2,7-dimethyl-,  
(2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 338999-26-1  
CMF C18 H21 N O



C

CM 2

CRN 110-16-7

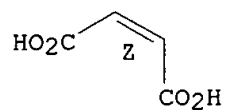
Brenda Coleman

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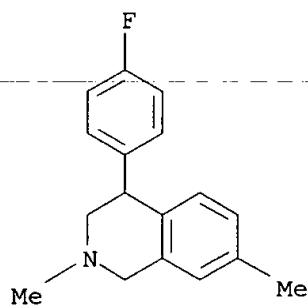
CMF C4 H4 O4

Double bond geometry as shown.



RN 338999-28-3 CAPLUS

CN Isoquinoline, 4-(4-fluorophenyl)-1,2,3,4-tetrahydro-2,7-dimethyl- (9CI)  
(CA INDEX NAME)



C

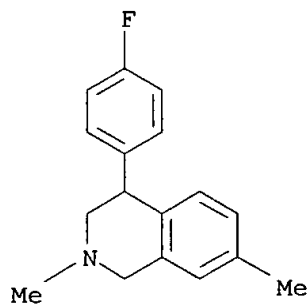
RN 338999-29-4 CAPLUS

CN Isoquinoline, 4-(4-fluorophenyl)-1,2,3,4-tetrahydro-2,7-dimethyl-,  
(2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 338999-28-3

CMF C17 H18 F N



C

CM 2

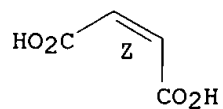
CRN 110-16-7

CMF C4 H4 O4

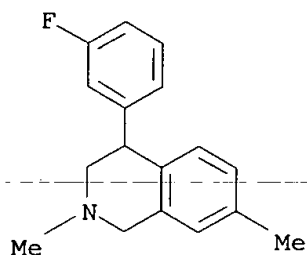
Double bond geometry as shown.

Brenda Coleman

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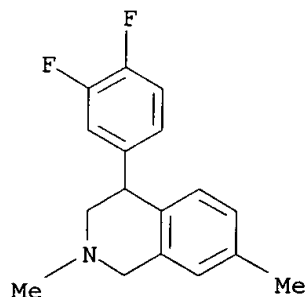


RN 338999-30-7 CAPLUS  
 CN Isoquinoline, 4-(3-fluorophenyl)-1,2,3,4-tetrahydro-2,7-dimethyl- (9CI)  
 (CA INDEX NAME)



C, E

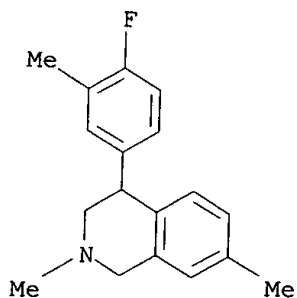
RN 338999-31-8 CAPLUS  
 CN Isoquinoline, 4-(3,4-difluorophenyl)-1,2,3,4-tetrahydro-2,7-dimethyl-,  
 hydrochloride (9CI) (CA INDEX NAME)



C, E

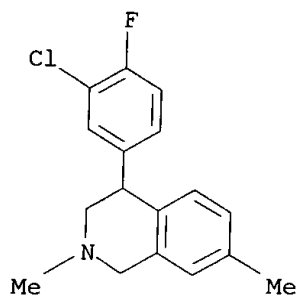
● HCl

RN 338999-32-9 CAPLUS  
 CN Isoquinoline, 4-(4-fluoro-3-methylphenyl)-1,2,3,4-tetrahydro-2,7-dimethyl-  
 (9CI) (CA INDEX NAME)



C,E

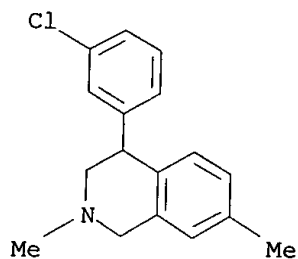
RN 338999-33-0 CAPLUS  
CN Isoquinoline, 4-(3-chloro-4-fluorophenyl)-1,2,3,4-tetrahydro-2,7-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



C,E

● HCl

RN 338999-34-1 CAPLUS  
CN Isoquinoline, 4-(3-chlorophenyl)-1,2,3,4-tetrahydro-2,7-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



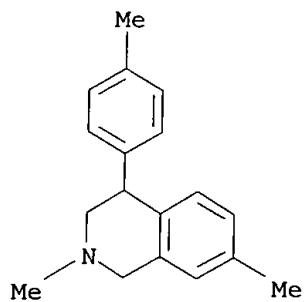
C,E

● HCl

RN 338999-35-2 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-2,7-dimethyl-4-(4-methylphenyl)-, hydrochloride (9CI) (CA INDEX NAME)

09/704,306

hydrochloride (9CI) (CA INDEX NAME)

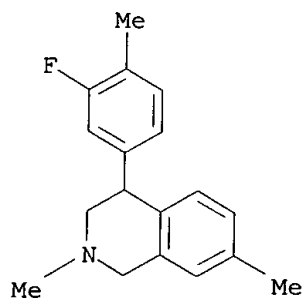


C

● HCl

RN 338999-36-3 CAPLUS

CN Isoquinoline, 4-(3-fluoro-4-methylphenyl)-1,2,3,4-tetrahydro-2,7-dimethyl-  
, hydrochloride (9CI) (CA INDEX NAME)



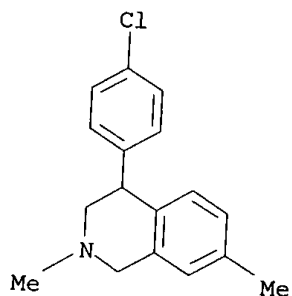
C, E

● HCl

RN 338999-37-4 CAPLUS

CN Isoquinoline, 4-(4-chlorophenyl)-1,2,3,4-tetrahydro-2,7-dimethyl- (9CI)  
(CA INDEX NAME)

09/704,306

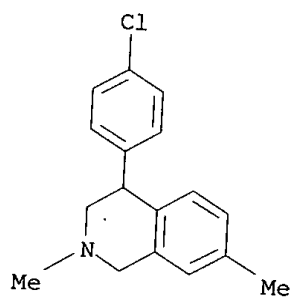


C

RN 338999-38-5 CAPLUS  
CN Isoquinoline, 4-(4-chlorophenyl)-1,2,3,4-tetrahydro-2,7-dimethyl-,  
(2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 338999-37-4  
CMF C17 H18 Cl N

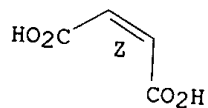


C

CM 2

CRN 110-16-7  
CMF C4 H4 O4

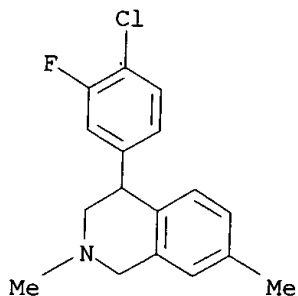
Double bond geometry as shown.



RN 338999-39-6 CAPLUS  
CN Isoquinoline, 4-(4-chloro-3-fluorophenyl)-1,2,3,4-tetrahydro-2,7-dimethyl-,  
hydrochloride (9CI) (CA INDEX NAME)

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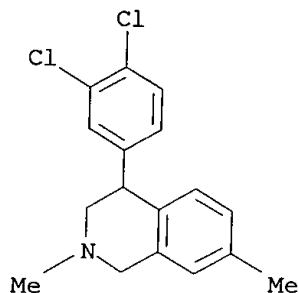
<page



C,E

● HCl

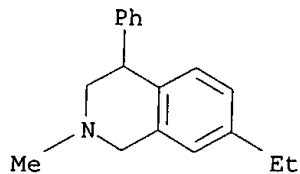
RN 338999-40-9 CAPLUS  
CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-2,7-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



C,E

● HCl

RN 338999-41-0 CAPLUS  
CN Isoquinoline, 7-ethyl-1,2,3,4-tetrahydro-2-methyl-4-phenyl-, INDEX NAME) (9CI) (CA



C

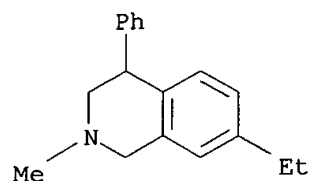
RN 338999-42-1 CAPLUS  
CN Isoquinoline, 7-ethyl-1,2,3,4-tetrahydro-2-methyl-4-phenyl-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1



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CRN 338999-41-0  
CMF C18 H21 N

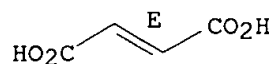


C

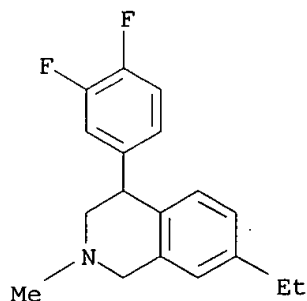
CM 2

CRN 110-17-8  
CMF C4 H4 O4

Double bond geometry as shown.



RN 338999-43-2 CAPLUS  
CN Isoquinoline, 4-(3,4-difluorophenyl)-7-ethyl-1,2,3,4-tetrahydro-2-methyl-  
(9CI) (CA INDEX NAME)



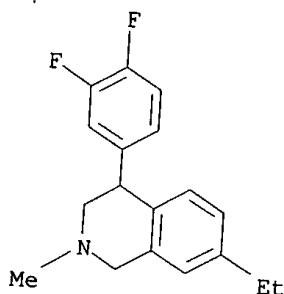
C, E

RN 338999-44-3 CAPLUS  
CN Isoquinoline, 4-(3,4-difluorophenyl)-7-ethyl-1,2,3,4-tetrahydro-2-methyl-,  
(2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 338999-43-2  
CMF C18 H19 F2 N

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CM 2

CRN 110-17-8

CMF C4 H4 O4

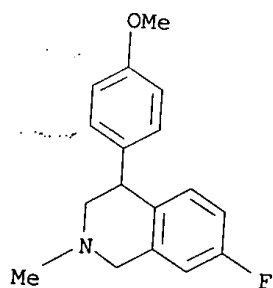
C<sub>1</sub>E

Double bond geometry as shown.



RN 338999-45-4 CAPLUS

CN Isoquinoline, 7-fluoro-1,2,3,4-tetrahydro-4-(4-methoxyphenyl)-2-methyl-  
(9CI) (CA INDEX NAME)



exc.

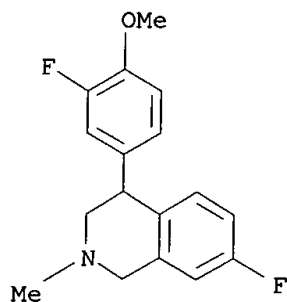
RN 338999-46-5 CAPLUS

CN Isoquinoline, 7-fluoro-4-(3-fluoro-4-methoxyphenyl)-1,2,3,4-tetrahydro-2-  
methyl-, hydrochloride (9CI) (CA INDEX NAME)

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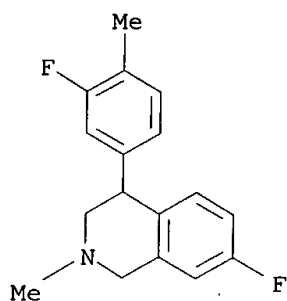


E

● HCl

RN 338999-47-6 CAPLUS

CN Isoquinoline, 7-fluoro-4-(3-fluoro-4-methylphenyl)-1,2,3,4-tetrahydro-2-methyl-, hydrochloride (9CI) (CA INDEX NAME)

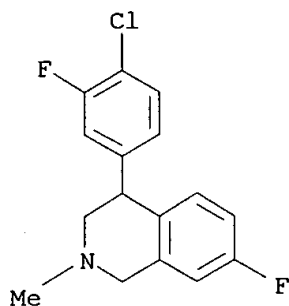


E

● HCl

RN 338999-48-7 CAPLUS

CN Isoquinoline, 4-(4-chloro-3-fluorophenyl)-7-fluoro-1,2,3,4-tetrahydro-2-methyl-, hydrochloride (9CI) (CA INDEX NAME)

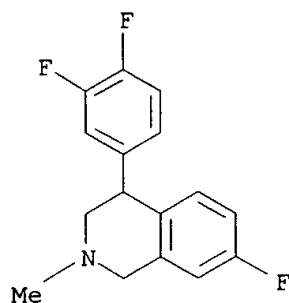


E

● HCl

---

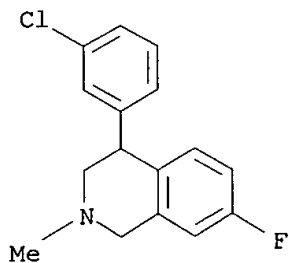
RN 338999-49-8 CAPLUS  
 CN Isoquinoline, 4-(3,4-difluorophenyl)-7-fluoro-1,2,3,4-tetrahydro-2-methyl-, hydrochloride (9CI) (CA INDEX NAME)



E

● HCl

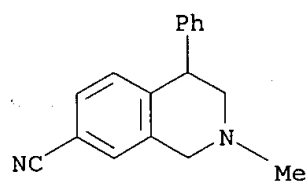
RN 338999-50-1 CAPLUS  
 CN Isoquinoline, 4-(3-chlorophenyl)-7-fluoro-1,2,3,4-tetrahydro-2-methyl-, hydrochloride (9CI) (CA INDEX NAME)



E

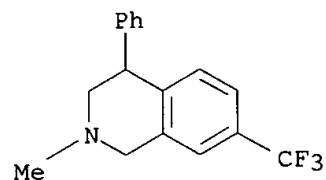
● HCl

RN 338999-51-2 CAPLUS  
CN 7-Isoquinolinecarbonitrile, 1,2,3,4-tetrahydro-2-methyl-4-phenyl- (9CI)  
(CA INDEX NAME)



exC

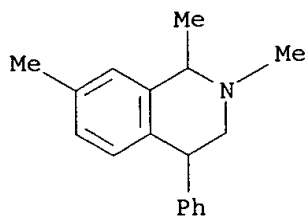
RN 338999-52-3 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-2-methyl-4-phenyl-7-(trifluoromethyl)-,  
hydrochloride (9CI) (CA INDEX NAME)



C

● HCl

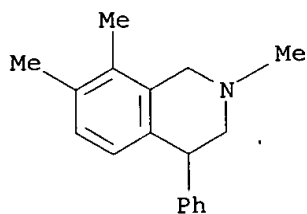
RN 338999-53-4 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-1,2,7-trimethyl-4-phenyl-, hydrochloride  
(9CI) (CA INDEX NAME)



C

● HCl

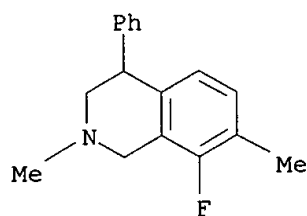
RN 338999-56-7 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-2,7,8-trimethyl-4-phenyl-, hydrochloride  
(9CI) (CA INDEX NAME)



C

● HCl

RN 338999-57-8 CAPLUS  
CN Isoquinoline, 8-fluoro-1,2,3,4-tetrahydro-2,7-dimethyl-4-phenyl-,  
hydrochloride (9CI) (CA INDEX NAME)

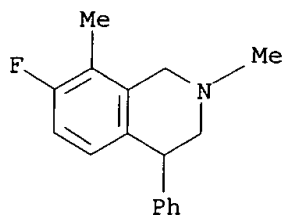


C

● HCl

RN 338999-58-9 CAPLUS  
CN Isoquinoline, 7-fluoro-1,2,3,4-tetrahydro-2,8-dimethyl-4-phenyl- (9CI)  
(CA INDEX NAME)

09/704,306

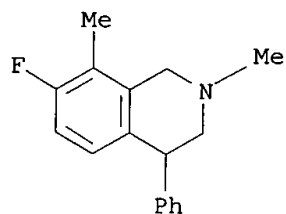


A

RN 338999-59-0 CAPLUS  
CN Isoquinoline, 7-fluoro-1,2,3,4-tetrahydro-2,8-dimethyl-4-phenyl-,  
(2E)-2-butenedioate (2:3) (9CI) (CA INDEX NAME)

CM 1

CRN 338999-58-9  
CMF C17 H18 F N

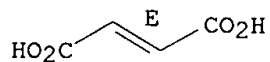


A

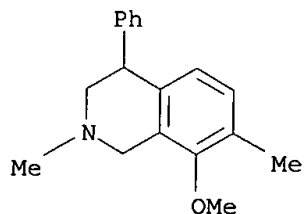
CM 2

CRN 110-17-8  
CMF C4 H4 O4

Double bond geometry as shown.



RN 338999-60-3 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-8-methoxy-2,7-dimethyl-4-phenyl- (9CI)  
(CA INDEX NAME)



C

RN 338999-61-4 CAPLUS

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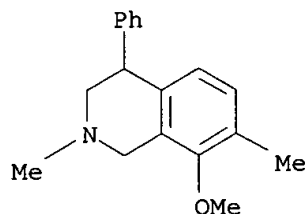
09/704,306

CN Isoquinoline, 1,2,3,4-tetrahydro-8-methoxy-2,7-dimethyl-4-phenyl-,  
(2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 338999-60-3

CMF C18 H21 N O



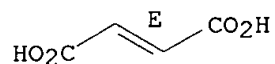
C

CM 2

CRN 110-17-8

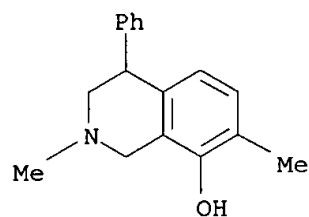
CMF C4 H4 O4

Double bond geometry as shown.



RN 338999-62-5 CAPLUS

CN 8-Isoquinolinol, 1,2,3,4-tetrahydro-2,7-dimethyl-4-phenyl-, hydrobromide  
(9CI) (CA INDEX NAME)



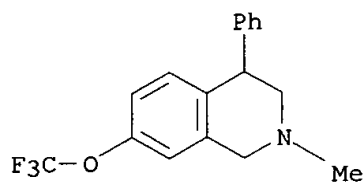
C

● HBr

RN 338999-63-6 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-2-methyl-4-phenyl-7-(trifluoromethoxy)-  
(9CI) (CA INDEX NAME)



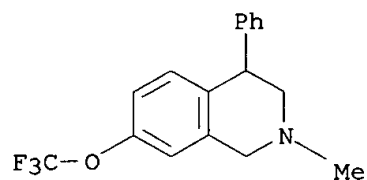


etc

RN 338999-64-7 CAPLUS  
 CN Isoquinoline, 1,2,3,4-tetrahydro-2-methyl-4-phenyl-7-(trifluoromethoxy)-,  
 (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 338999-63-6  
 CMF C17 H16 F3 N O

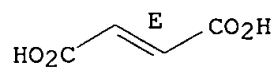


etc

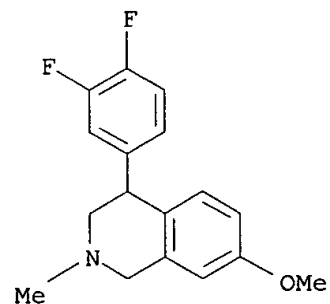
CM 2

CRN 110-17-8  
 CMF C4 H4 O4

Double bond geometry as shown.



RN 338999-65-8 CAPLUS  
 CN Isoquinoline, 4-(3,4-difluorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-  
 (9CI) (CA INDEX NAME)

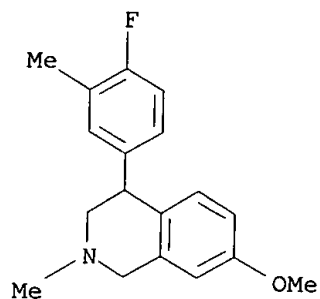


E

RN 338999-66-9 CAPLUS

09/704,306

CN Isoquinoline, 4-(4-fluoro-3-methylphenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-, hydrochloride (9CI) (CA INDEX NAME)

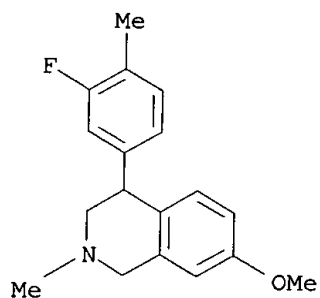


E

● HCl

RN 338999-67-0 CAPLUS

CN Isoquinoline, 4-(3-fluoro-4-methylphenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl- (9CI) (CA INDEX NAME)



E

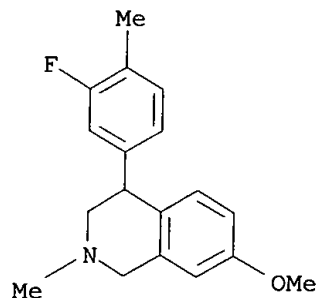
RN 338999-68-1 CAPLUS

CN Isoquinoline, 4-(3-fluoro-4-methylphenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 338999-67-0

CMF C18 H20 F N O

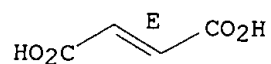


CM 2

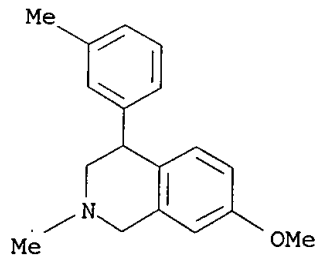
CRN 110-17-8

CMF C4 H4 O4

Double bond geometry as shown.



RN 338999-69-2 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-(3-methylphenyl)-  
(9CI) (CA INDEX NAME)

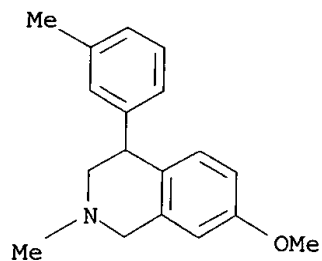
RN 338999-70-5 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-(3-methylphenyl)-,  
(2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 338999-69-2

CMF C18 H21 N O



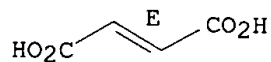
E

CM 2

CRN 110-17-8

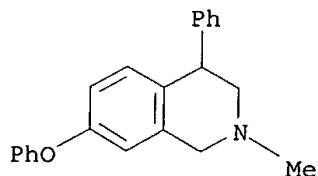
CMF C4 H4 O4

-----Double-bond geometry as shown.



RN 338999-71-6 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-2-methyl-7-phenoxy-4-phenyl- (9CI) (CA INDEX NAME)



P

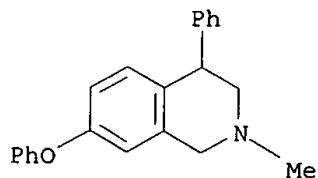
RN 338999-72-7 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-2-methyl-7-phenoxy-4-phenyl-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 338999-71-6

CMF C22 H21 N O



D

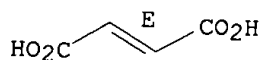
CM 2

09/704,306

CRN 110-17-8

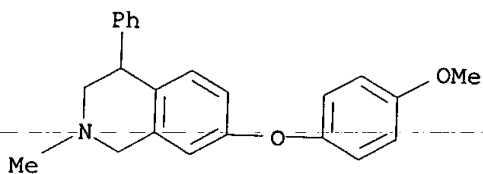
CMF C4 H4 O4

Double bond geometry as shown.



RN 338999-73-8 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-7-(4-methoxyphenoxy)-2-methyl-4-phenyl-  
(9CI) (CA INDEX NAME)



D

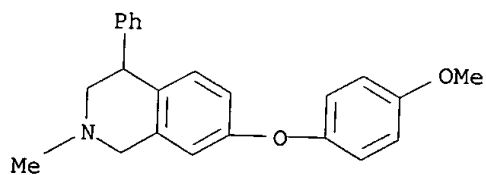
RN 338999-74-9 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-7-(4-methoxyphenoxy)-2-methyl-4-phenyl-,  
(2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 338999-73-8

CMF C23 H23 N O2



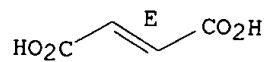
D

CM 2

CRN 110-17-8

CMF C4 H4 O4

Double bond geometry as shown.

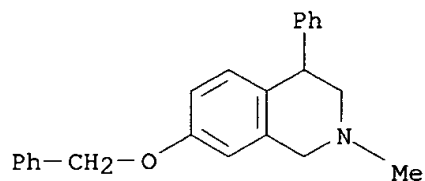


RN 338999-75-0 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-2-methyl-4-phenyl-7-(phenylmethoxy)-  
(9CI) (CA INDEX NAME)

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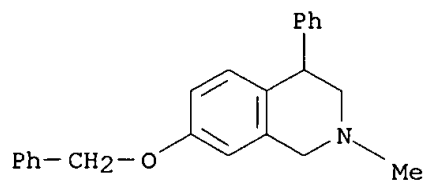


P

RN 338999-76-1 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-2-methyl-4-phenyl-7-(phenylmethoxy)-,  
(2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 338999-75-0  
CMF C23 H23 N O

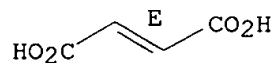


P

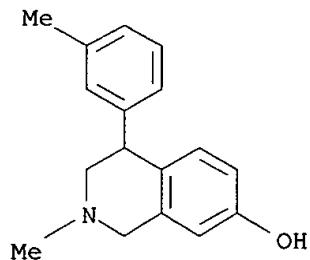
CM 2

CRN 110-17-8  
CMF C4 H4 O4

Double bond geometry as shown.



RN 338999-77-2 CAPLUS  
CN 7-Isoquinolinol, 1,2,3,4-tetrahydro-2-methyl-4-(3-methylphenyl)-,  
hydrochloride (9CI) (CA INDEX NAME)



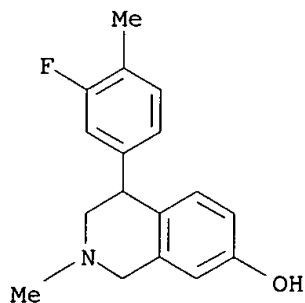
E

HCl

09/704,306

RN 338999-78-3 CAPLUS

CN 7-Isoquinolinol, 4-(3-fluoro-4-methylphenyl)-1,2,3,4-tetrahydro-2-methyl-  
(9CI) (CA INDEX NAME)



E

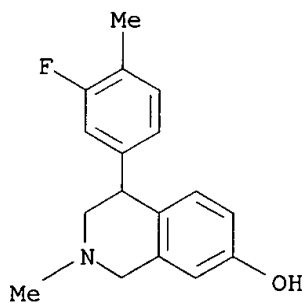
RN 338999-79-4 CAPLUS

CN 7-Isoquinolinol, 4-(3-fluoro-4-methylphenyl)-1,2,3,4-tetrahydro-2-methyl-,  
(2Z)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 338999-78-3

CMF C17 H18 F N O



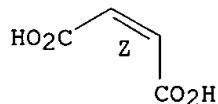
E

CM 2

CRN 110-16-7

CMF C4 H4 O4

Double bond geometry as shown.



RN 338999-80-7 CAPLUS

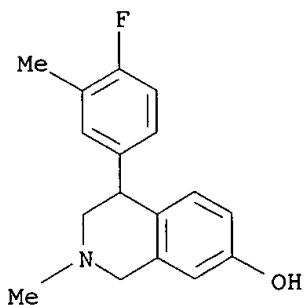
CN 7-Isoquinolinol, 4-(4-fluoro-3-methylphenyl)-1,2,3,4-tetrahydro-2-methyl-

Brenda Coleman

<page

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(9CI) (CA INDEX NAME)

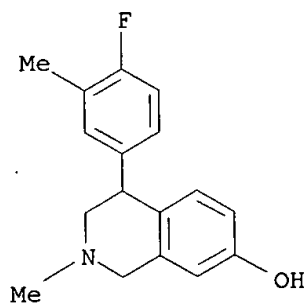


E

RN 338999-81-8 CAPLUS  
CN 7-Isoquinolinol, 4-(4-fluoro-3-methylphenyl)-1,2,3,4-tetrahydro-2-methyl-,  
----- (2Z)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME) -----

CM 1

CRN 338999-80-7  
CMF C17 H18 F N O

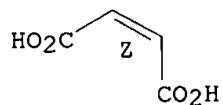


E

CM 2

CRN 110-16-7  
CMF C4 H4 O4

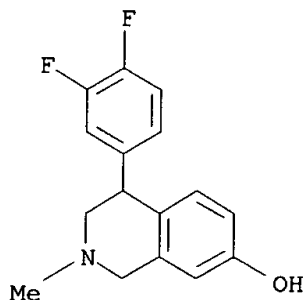
Double bond geometry as shown.



RN 338999-82-9 CAPLUS  
CN 7-Isoquinolinol, 4-(3,4-difluorophenyl)-1,2,3,4-tetrahydro-2-methyl-,  
hydrobromide (9CI) (CA INDEX NAME)



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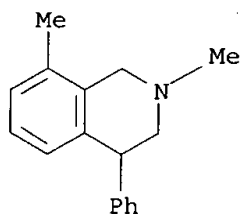


E

● HBr

RN 338999-84-1 CAPLUS

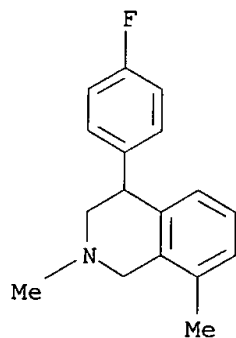
-----CN----- Isoquinoline, 1,2,3,4-tetrahydro-2,8-dimethyl-4-phenyl- (9CI) (CA INDEX NAME)



A

RN 338999-85-2 CAPLUS

CN Isoquinoline, 4-(4-fluorophenyl)-1,2,3,4-tetrahydro-2,8-dimethyl- (9CI)  
(CA INDEX NAME)



A

RN 338999-86-3 CAPLUS

CN Isoquinoline, 4-(4-fluorophenyl)-1,2,3,4-tetrahydro-2,8-dimethyl-,  
(2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

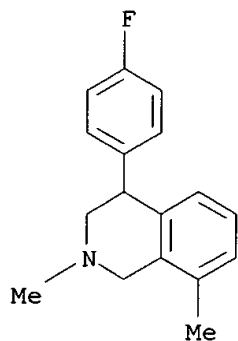
CRN 338999-85-2

Brenda Coleman

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09/704,306

CMF C17 H18 F N

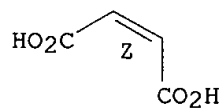


A

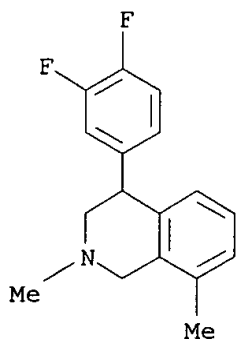
CM 2

CRN 110-16-7  
CMF C4 H4 O4

Double bond geometry as shown.



RN 338999-87-4 CAPLUS  
CN Isoquinoline, 4-(3,4-difluorophenyl)-1,2,3,4-tetrahydro-2,8-dimethyl-,  
hydrochloride (9CI) (CA INDEX NAME)



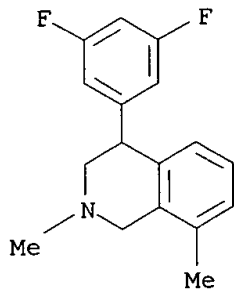
A, E

● HCl

RN 338999-88-5 CAPLUS  
CN Isoquinoline, 4-(3,5-difluorophenyl)-1,2,3,4-tetrahydro-2,8-dimethyl-,  
hydrochloride (9CI) (CA INDEX NAME)

Brenda Coleman

<page

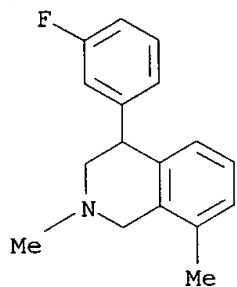


AE

● HCl

RN 338999-89-6 CAPLUS

CN Isoquinoline, 4-(3-fluorophenyl)-1,2,3,4-tetrahydro-2,8-dimethyl- (9CI)  
(CA INDEX NAME)



AE

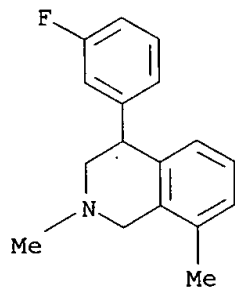
RN 338999-90-9 CAPLUS

CN Isoquinoline, 4-(3-fluorophenyl)-1,2,3,4-tetrahydro-2,8-dimethyl-,  
(2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 338999-89-6

CMF C17 H18 F N



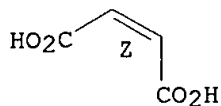
AE

CM 2

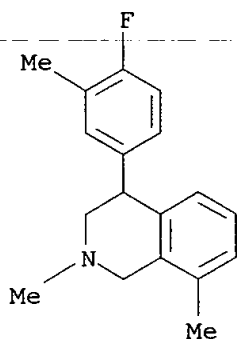
09/704,306

CRN 110-16-7  
CMF C4 H4 O4

Double bond geometry as shown.

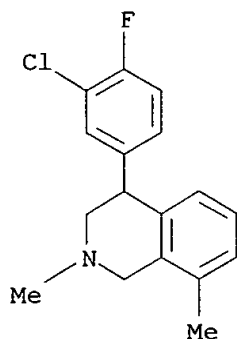


RN 338999-92-1 CAPLUS  
CN Isoquinoline, 4-(4-fluoro-3-methylphenyl)-1,2,3,4-tetrahydro-2,8-dimethyl-  
(9CI) (CA INDEX NAME)



AE

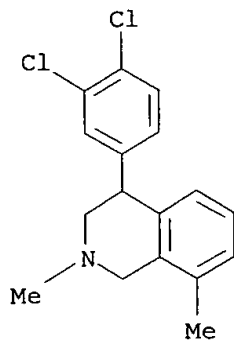
RN 338999-94-3 CAPLUS  
CN Isoquinoline, 4-(3-chloro-4-fluorophenyl)-1,2,3,4-tetrahydro-2,8-dimethyl-,  
hydrochloride (9CI) (CA INDEX NAME)



AE

● HCl

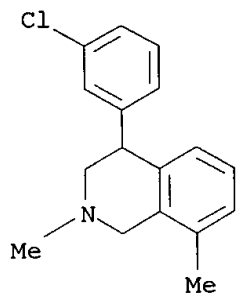
RN 338999-95-4 CAPLUS  
CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-2,8-dimethyl-,  
hydrochloride (9CI) (CA INDEX NAME)



AE

● HCl

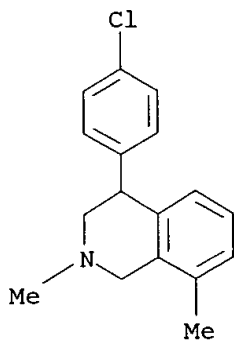
RN 338999-96-5 CAPLUS  
CN Isoquinoline, 4-(3-chlorophenyl)-1,2,3,4-tetrahydro-2,8-dimethyl-,  
hydrochloride (9CI) (CA INDEX NAME)



AE

● HCl

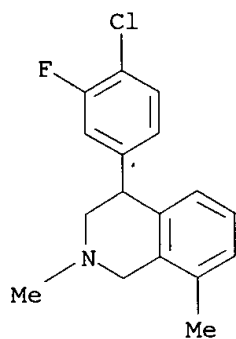
RN 338999-97-6 CAPLUS  
CN Isoquinoline, 4-(4-chlorophenyl)-1,2,3,4-tetrahydro-2,8-dimethyl-,  
hydrochloride (9CI) (CA INDEX NAME)



A

● HCl

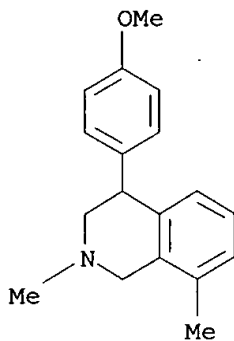
RN 338999-98-7 CAPLUS  
CN Isoquinoline, 4-(4-chloro-3-fluorophenyl)-1,2,3,4-tetrahydro-2,8-dimethyl-  
, hydrochloride (9CI) (CA INDEX NAME)



AE

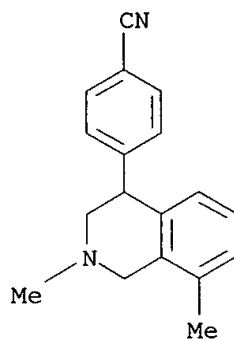
● HCl

RN 338999-99-8 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-4-(4-methoxyphenyl)-2,8-dimethyl- (9CI)  
(CA INDEX NAME)



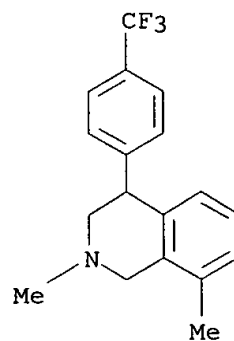
A

RN 339000-00-9 CAPLUS  
 CN Benzonitrile, 4-(1,2,3,4-tetrahydro-2,8-dimethyl-4-isoquinolinyl)- (9CI)  
 (CA INDEX NAME)



A

RN 339000-01-0 CAPLUS  
 CN Isoquinoline, 1,2,3,4-tetrahydro-2,8-dimethyl-4-[4-(trifluoromethyl)phenyl]-, hydrochloride (9CI) (CA INDEX NAME)



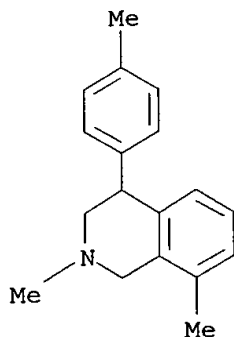
A

● HCl

RN 339000-02-1 CAPLUS

09/704,306

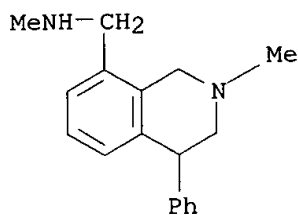
CN Isoquinoline, 1,2,3,4-tetrahydro-2,8-dimethyl-4-(4-methylphenyl)- (9CI)  
(CA INDEX NAME)



A

RN 339000-03-2 CAPLUS

CN 8-Isoquinolinemethanamine, 1,2,3,4-tetrahydro-N,2-dimethyl-4-phenyl-,  
monohydrochloride (9CI) (CA INDEX NAME)

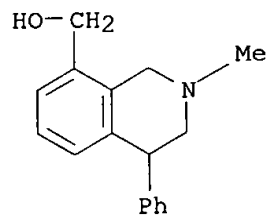


A

● HCl

RN 339000-04-3 CAPLUS

CN 8-Isoquinolinemethanol, 1,2,3,4-tetrahydro-2-methyl-4-phenyl- (9CI) (CA  
INDEX NAME)

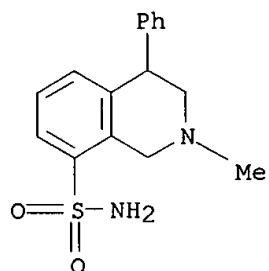


A

RN 339000-05-4 CAPLUS

CN 8-Isoquinolinesulfonamide, 1,2,3,4-tetrahydro-2-methyl-4-phenyl- (9CI)  
(CA INDEX NAME)

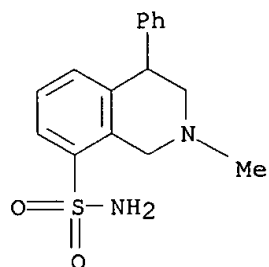




RN 339000-06-5 CAPLUS  
 CN 8-Isoquinolinesulfonamide, 1,2,3,4-tetrahydro-2-methyl-4-phenyl-,  
 (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

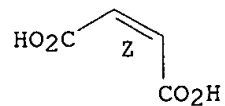
CRN 339000-05-4  
 CMF C16 H18 N2 O2 S



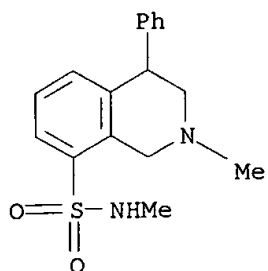
CM 2

CRN 110-16-7  
 CMF C4 H4 O4

Double bond geometry as shown.



RN 339000-07-6 CAPLUS  
 CN 8-Isoquinolinesulfonamide, 1,2,3,4-tetrahydro-N,2-dimethyl-4-phenyl-,  
 monohydrochloride (9CI) (CA INDEX NAME)

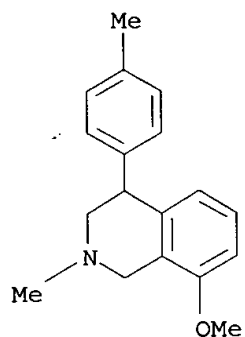


B

● HCl

RN 339000-08-7 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-8-methoxy-2-methyl-4-(4-methylphenyl)-, hydrochloride (9CI) (CA INDEX NAME)

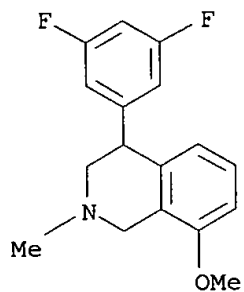


exc

● HCl

RN 339000-09-8 CAPLUS

CN Isoquinoline, 4-(3,5-difluorophenyl)-1,2,3,4-tetrahydro-8-methoxy-2-methyl- (9CI) (CA INDEX NAME)



E

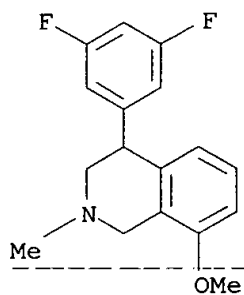
RN 339000-10-1 CAPLUS

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CN Isoquinoline, 4-(3,5-difluorophenyl)-1,2,3,4-tetrahydro-8-methoxy-2-methyl-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

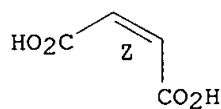
CRN 339000-09-8  
CMF C17 H17 F2 N O



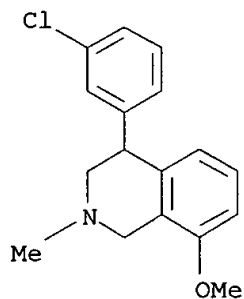
CM 2

CRN 110-16-7  
CMF C4 H4 O4

Double bond geometry as shown.



RN 339000-11-2 CAPLUS  
CN Isoquinoline, 4-(3-chlorophenyl)-1,2,3,4-tetrahydro-8-methoxy-2-methyl-, (9CI) (CA INDEX NAME)

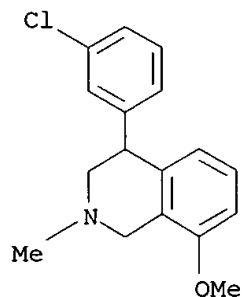


RN 339000-12-3 CAPLUS  
CN Isoquinoline, 4-(3-chlorophenyl)-1,2,3,4-tetrahydro-8-methoxy-2-methyl-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

09/704,306

CRN 339000-11-2  
CMF C17 H18 Cl N O

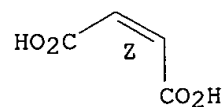


E

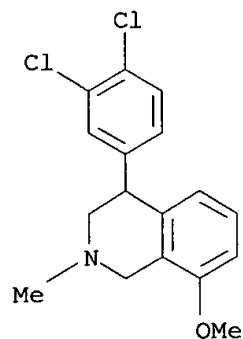
CM 2

CRN 110-16-7  
CMF C4 H4 O4

Double bond geometry as shown.



RN 339000-13-4 CAPLUS  
CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-8-methoxy-2-methyl-, hydrochloride (9CI) (CA INDEX NAME)

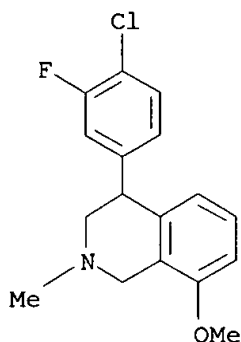


E

● HCl

RN 339000-14-5 CAPLUS  
CN Isoquinoline, 4-(4-chloro-3-fluorophenyl)-1,2,3,4-tetrahydro-8-methoxy-2-methyl- (9CI) (CA INDEX NAME)

09/704,306

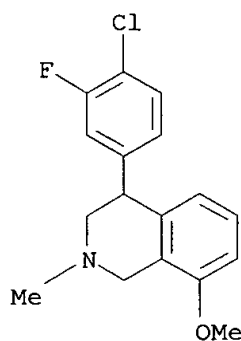


E

RN 339000-15-6 CAPLUS  
CN Isoquinoline, 4-(4-chloro-3-fluorophenyl)-1,2,3,4-tetrahydro-8-methoxy-2-methyl-, sulfate (1:1) (9CI) (CA INDEX NAME)

CM 1

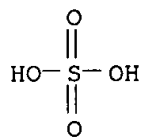
CRN 339000-14-5  
CMF C17 H17 Cl F N O



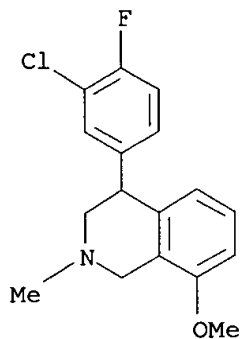
E

CM 2

CRN 7664-93-9  
CMF H2 O4 S



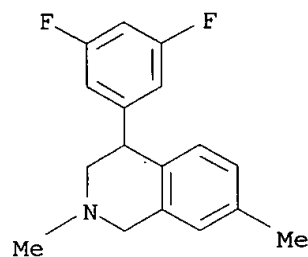
RN 339000-16-7 CAPLUS  
CN Isoquinoline, 4-(3-chloro-4-fluorophenyl)-1,2,3,4-tetrahydro-8-methoxy-2-methyl-, hydrochloride (9CI) (CA INDEX NAME)



E

● HCl

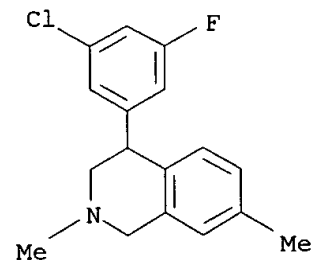
RN 339000-19-0 CAPLUS  
 CN Isoquinoline, 4-(3,5-difluorophenyl)-1,2,3,4-tetrahydro-2,7-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



C, E

● HCl

RN 339000-20-3 CAPLUS  
 CN Isoquinoline, 4-(3-chloro-5-fluorophenyl)-1,2,3,4-tetrahydro-2,7-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

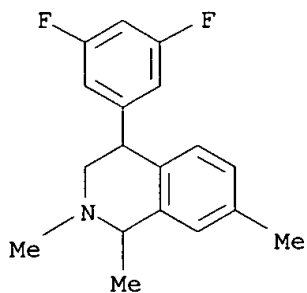


C, E

HCl

RN 339000-32-7 CAPLUS

CN Isoquinoline, 4-(3,5-difluorophenyl)-1,2,3,4-tetrahydro-1,2,7-trimethyl-,  
hydrochloride (9CI) (CA INDEX NAME)

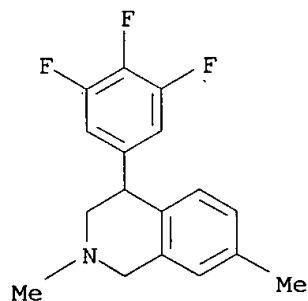


CE

● HCl

RN 339000-33-8 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-2,7-dimethyl-4-(3,4,5-trifluorophenyl)-,  
hydrochloride (9CI) (CA INDEX NAME)

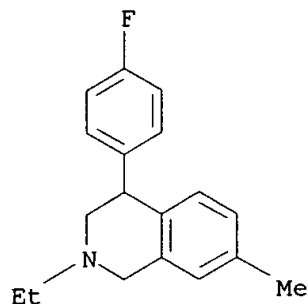


CE

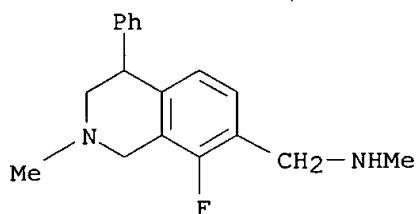
● HCl

RN 339000-34-9 CAPLUS

CN Isoquinoline, 2-ethyl-4-(4-fluorophenyl)-1,2,3,4-tetrahydro-7-methyl-  
(9CI) (CA INDEX NAME)



RN 339000-36-1 CAPLUS  
 CN 7-Isoquinolinemethanamine, 8-fluoro-1,2,3,4-tetrahydro-N,2-dimethyl-4-phenyl-, dihydrochloride (9CI) (CA INDEX NAME)

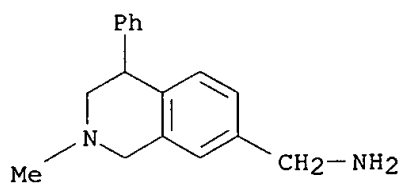


● 2 HCl

RN 339000-38-3 CAPLUS  
 CN 7-Isoquinolinemethanamine, 1,2,3,4-tetrahydro-2-methyl-4-phenyl-, (2Z)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 339000-37-2  
 CMF C17 H20 N2



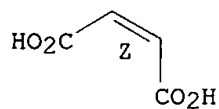
CM 2

CRN 110-16-7  
 CMF C4 H4 O4

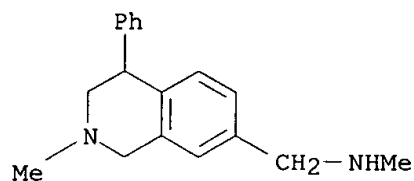
Double bond geometry as shown.



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RN 339000-39-4 CAPLUS  
CN 7-Isoquinolinemethanamine, 1,2,3,4-tetrahydro-N,2-dimethyl-4-phenyl- (9CI)  
(CA INDEX NAME)

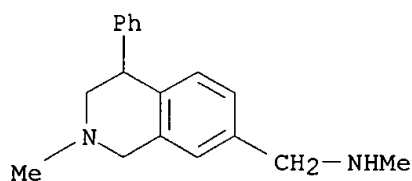


C

RN 339000-40-7 CAPLUS  
CN 7-Isoquinolinemethanamine, 1,2,3,4-tetrahydro-N,2-dimethyl-4-phenyl-,  
(2Z)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 339000-39-4  
CMF C18 H22 N2

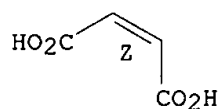


C

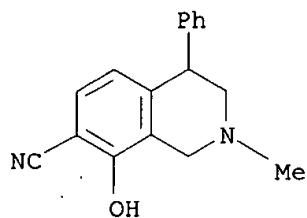
CM 2

CRN 110-16-7  
CMF C4 H4 O4

Double bond geometry as shown.

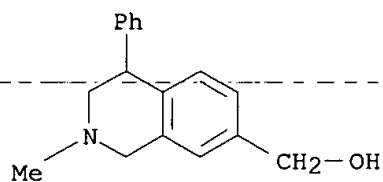


RN 339000-41-8 CAPLUS  
CN 7-Isoquinolinecarbonitrile, 1,2,3,4-tetrahydro-8-hydroxy-2-methyl-4-phenyl-  
(9CI) (CA INDEX NAME)



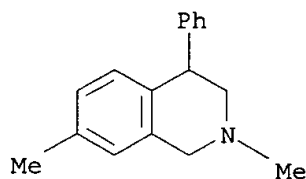
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RN 339000-42-9 CAPLUS  
CN 7-Isoquinolinemethanol, 1,2,3,4-tetrahydro-2-methyl-4-phenyl- (9CI) (CA INDEX NAME)



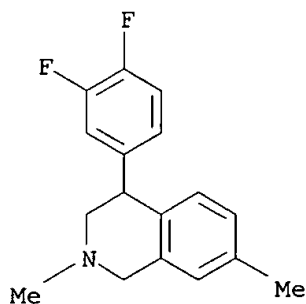
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RN 339000-44-1 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-2,7-dimethyl-4-phenyl- (9CI) (CA INDEX NAME)



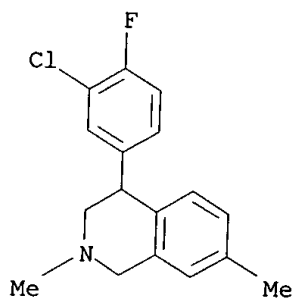
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RN 339000-45-2 CAPLUS  
CN Isoquinoline, 4-(3,4-difluorophenyl)-1,2,3,4-tetrahydro-2,7-dimethyl- (9CI) (CA INDEX NAME)



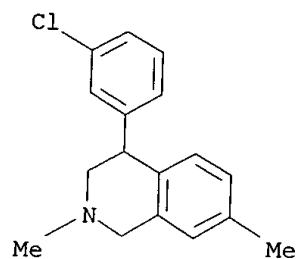
CE

RN 339000-46-3 CAPLUS  
CN Isoquinoline, 4-(3-chloro-4-fluorophenyl)-1,2,3,4-tetrahydro-2,7-dimethyl- (9CI) (CA INDEX NAME)



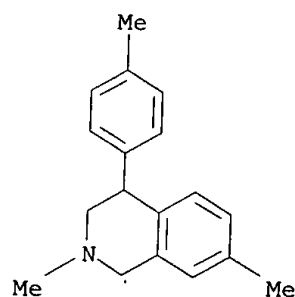
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RN 339000-47-4 CAPLUS  
CN Isoquinoline, 4-(3-chlorophenyl)-1,2,3,4-tetrahydro-2,7-dimethyl- (9CI)  
(CA INDEX NAME)



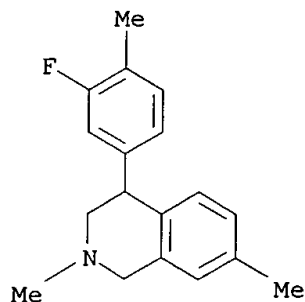
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RN 339000-48-5 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-2,7-dimethyl-4-(4-methylphenyl)- (9CI)  
(CA INDEX NAME)



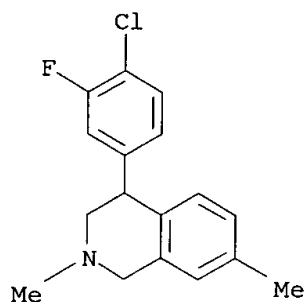
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RN 339000-49-6 CAPLUS  
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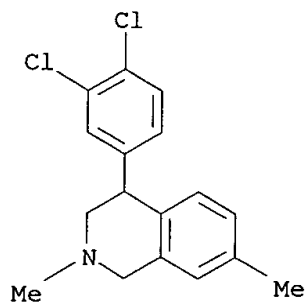
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RN 339000-50-9 CAPLUS  
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(9CI) (CA INDEX NAME)



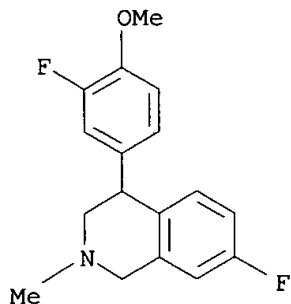
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RN 339000-51-0 CAPLUS  
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(9CI) (CA INDEX NAME)



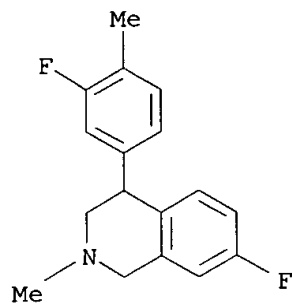
CE

RN 339000-52-1 CAPLUS  
CN Isoquinoline, 7-fluoro-4-(3-fluoro-4-methoxyphenyl)-1,2,3,4-tetrahydro-2-  
methyl- (9CI) (CA INDEX NAME)



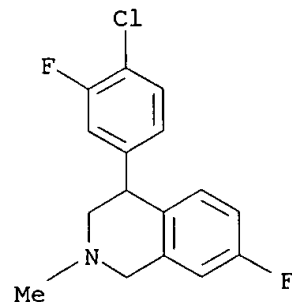
E

RN 339000-53-2 CAPLUS  
CN Isoquinoline, 7-fluoro-4-(3-fluoro-4-methylphenyl)-1,2,3,4-tetrahydro-2-methyl- (9CI) (CA INDEX NAME)



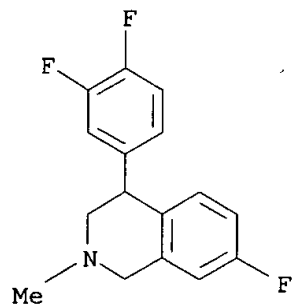
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RN 339000-54-3 CAPLUS  
CN Isoquinoline, 4-(4-chloro-3-fluorophenyl)-7-fluoro-1,2,3,4-tetrahydro-2-methyl- (9CI) (CA INDEX NAME)



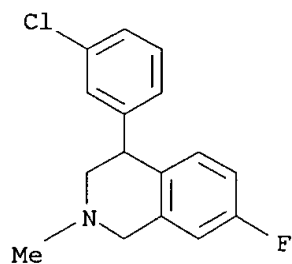
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RN 339000-55-4 CAPLUS  
CN Isoquinoline, 4-(3,4-difluorophenyl)-7-fluoro-1,2,3,4-tetrahydro-2-methyl- (9CI) (CA INDEX NAME)



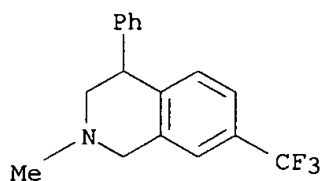
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RN 339000-56-5 CAPLUS  
CN Isoquinoline, 4-(3-chlorophenyl)-7-fluoro-1,2,3,4-tetrahydro-2-methyl-  
(9CI) (CA INDEX NAME)



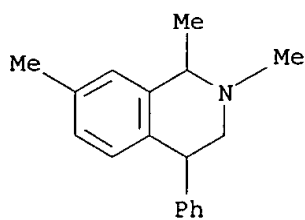
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RN 339000-57-6 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-2-methyl-4-phenyl-7-(trifluoromethyl)-  
(9CI) (CA INDEX NAME)



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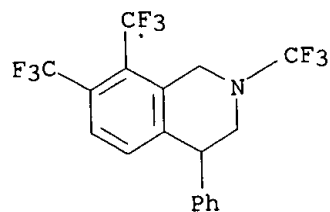
RN 339000-58-7 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-1,2,7-trimethyl-4-phenyl- (9CI) (CA  
INDEX NAME)



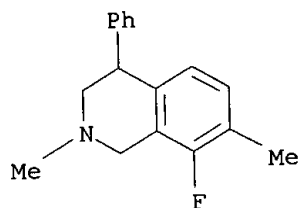
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09/704,306

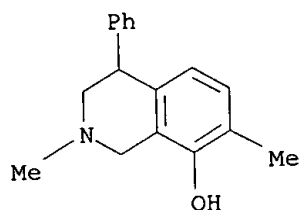
RN 339000-59-8 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-4-phenyl-2,7,8-tris(trifluoromethyl)-  
(9CI) (CA INDEX NAME)



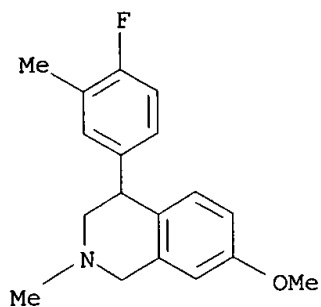
RN 339000-60-1 CAPLUS  
CN Isoquinoline, 8-fluoro-1,2,3,4-tetrahydro-2,7-dimethyl-4-phenyl- (9CI)  
(CA INDEX NAME)



RN 339000-61-2 CAPLUS  
CN 8-Isoquinolinol, 1,2,3,4-tetrahydro-2,7-dimethyl-4-phenyl- (9CI) (CA  
INDEX NAME)

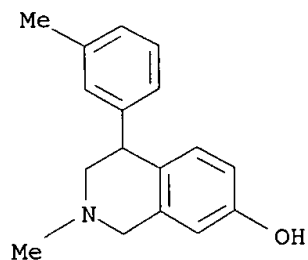


RN 339000-62-3 CAPLUS  
CN Isoquinoline, 4-(4-fluoro-3-methylphenyl)-1,2,3,4-tetrahydro-7-methoxy-2-  
methyl- (9CI) (CA INDEX NAME)



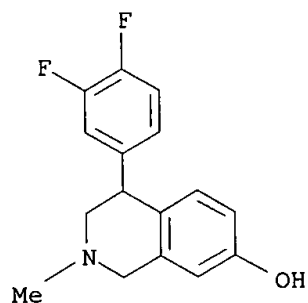
E

RN 339000-63-4 CAPLUS  
CN 7-Isoquinolinol, 1,2,3,4-tetrahydro-2-methyl-4-(3-methylphenyl)- (9CI)  
(CA INDEX NAME)



E

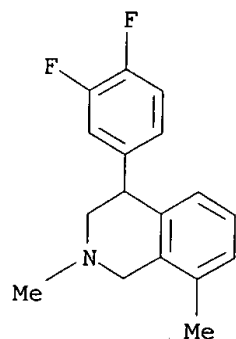
RN 339000-64-5 CAPLUS  
CN 7-Isoquinolinol, 4-(3,4-difluorophenyl)-1,2,3,4-tetrahydro-2-methyl- (9CI)  
(CA INDEX NAME)



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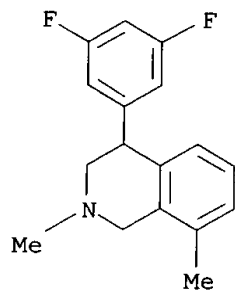
RN 339000-65-6 CAPLUS  
CN Isoquinoline, 4-(3,4-difluorophenyl)-1,2,3,4-tetrahydro-2,8-dimethyl-  
(9CI) (CA INDEX NAME)





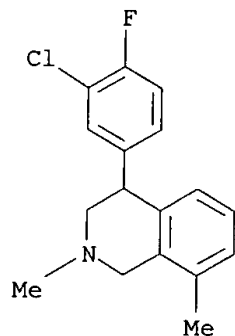
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RN 339000-66-7 CAPLUS  
CN Isoquinoline, 4-(3,5-difluorophenyl)-1,2,3,4-tetrahydro-2,8-dimethyl-  
(9CI) (CA INDEX NAME)



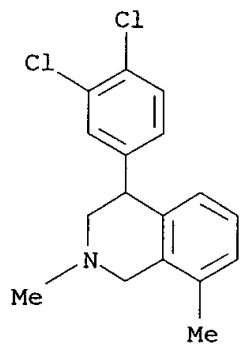
AE

RN 339000-67-8 CAPLUS  
CN Isoquinoline, 4-(3-chloro-4-fluorophenyl)-1,2,3,4-tetrahydro-2,8-dimethyl-  
(9CI) (CA INDEX NAME)



AE

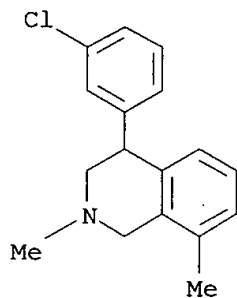
RN 339000-68-9 CAPLUS  
CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-2,8-dimethyl-  
(9CI) (CA INDEX NAME)



AE

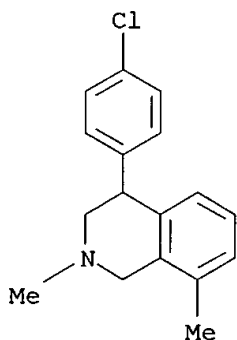
RN 339000-69-0 CAPLUS  
CN Isoquinoline, 4-(3-chlorophenyl)-1,2,3,4-tetrahydro-2,8-dimethyl- (9CI)  
(CA INDEX NAME)

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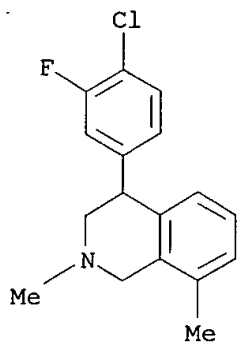
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RN 339000-70-3 CAPLUS  
CN Isoquinoline, 4-(4-chlorophenyl)-1,2,3,4-tetrahydro-2,8-dimethyl- (9CI)  
(CA INDEX NAME)



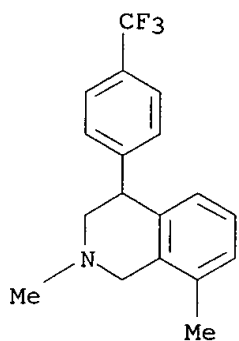
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RN 339000-71-4 CAPLUS  
CN Isoquinoline, 4-(4-chloro-3-fluorophenyl)-1,2,3,4-tetrahydro-2,8-dimethyl-  
(9CI) (CA INDEX NAME)



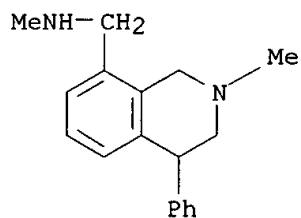
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RN 339000-72-5 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-2,8-dimethyl-4-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



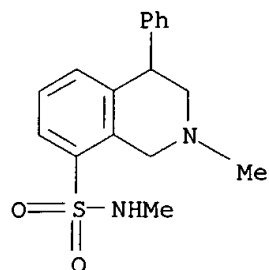
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RN 339000-73-6 CAPLUS  
CN 8-Isoquinolinemethanamine, 1,2,3,4-tetrahydro-N,2-dimethyl-4-phenyl- (9CI) (CA INDEX NAME)



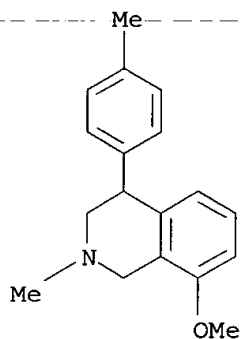
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RN 339000-74-7 CAPLUS  
CN 8-Isoquinolinesulfonamide, 1,2,3,4-tetrahydro-N,2-dimethyl-4-phenyl- (9CI) (CA INDEX NAME)



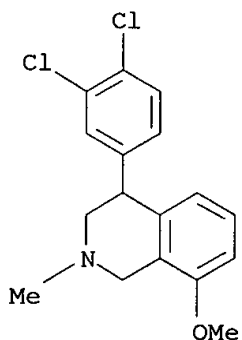
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RN 339000-75-8 CAPLUS  
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(9CI) (CA INDEX NAME)



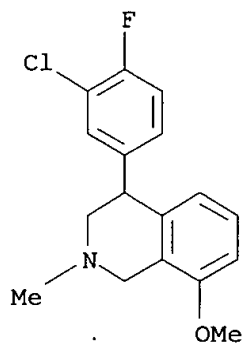
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RN 339000-76-9 CAPLUS  
CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-8-methoxy-2-methyl-  
(9CI) (CA INDEX NAME)



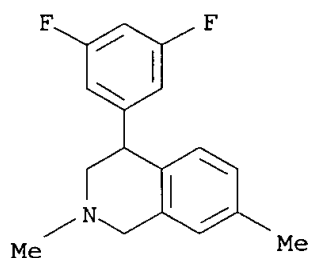
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RN 339000-77-0 CAPLUS  
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(9CI) (CA INDEX NAME)



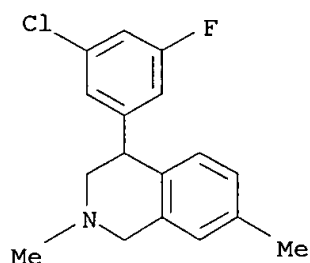
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RN 339000-80-5 CAPLUS  
CN Isoquinoline, 4-(3,5-difluorophenyl)-1,2,3,4-tetrahydro-2,7-dimethyl-  
(9CI) (CA INDEX NAME)



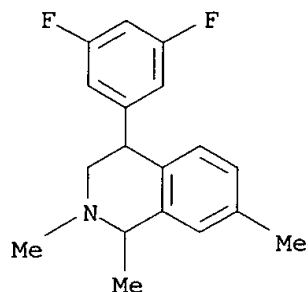
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RN 339000-81-6 CAPLUS  
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(9CI) (CA INDEX NAME)



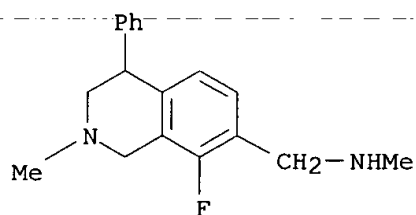
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RN 339000-89-4 CAPLUS  
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(9CI) (CA INDEX NAME)



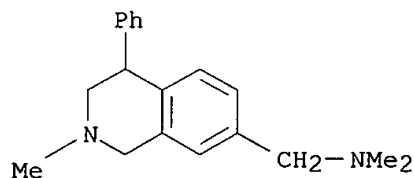
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RN 339000-90-7 CAPLUS  
CN 7-Isoquinolinemethanamine, 8-fluoro-1,2,3,4-tetrahydro-N,2-dimethyl-4-phenyl- (9CI) (CA INDEX NAME)



C

RN 339000-92-9 CAPLUS  
CN 7-Isoquinolinemethanamine, 1,2,3,4-tetrahydro-N,N,2-trimethyl-4-phenyl- (9CI) (CA INDEX NAME)



546-144

C

RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

✓  
 L48 ANSWER 4 OF 100 CAPLUS COPYRIGHT 2003 ACS

AN 1999:479626 CAPLUS

DN 131:280995

TI Quantitative Structure-Activity Relationship Modeling of Dopamine D1 Antagonists Using Comparative Molecular Field Analysis, Genetic Algorithms-Partial Least-Squares, and K Nearest Neighbor Methods

AU Hoffman, Brian; Cho, Sung Jin; Zheng, Weifan; Wyrick, Steven; Nichols, David E.; Mailman, Richard B.; Tropsha, Alexander

CS Division of Medicinal Chemistry and Natural Products School of Pharmacy and Departments of Psychiatry and Pharmacology, University of North Carolina, Chapel Hill, NC, 27599, USA

SO Journal of Medicinal Chemistry (1999), 42(17), 3217-3226  
 CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

AB Several quant. structure-activity relationship (QSAR) methods were applied to 29 chem. diverse D1 dopamine antagonists. In addn. to conventional 3D comparative mol. field anal. (CoMFA), cross-validated R2 guided region selection (q2-GRS) CoMFA (see ref. 1) was employed, as were two novel variable selection QSAR methods recently developed in one of our labs. These latter methods included genetic algorithm-partial least squares (GA-PLS) and K nearest neighbor (KNN) procedures (see refs. 2-4), which utilize 2D topol. descriptors of chem. structures. Each QSAR approach resulted in a highly predictive model, with cross-validated R2 (q2) values of 0.57 for CoMFA, 0.54 for q2-GRS, 0.73 for GA-PLS, and 0.79 for KNN. The success of all of the QSAR methods indicates the presence of an intrinsic structure-activity relationship in this group of compds. and affords more robust design and prediction of biol. activities of novel D1 ligands.

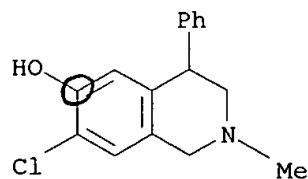
IT 115514-82-4

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(QSAR modeling of dopamine D1 antagonists using comparative mol. field anal., genetic algorithms-partial least-squares, and K nearest neighbor methods)

RN 115514-82-4 CAPLUS

CN 6-Isoquinolinol, 7-chloro-1,2,3,4-tetrahydro-2-methyl-4-phenyl- (9CI) (CA INDEX NAME)

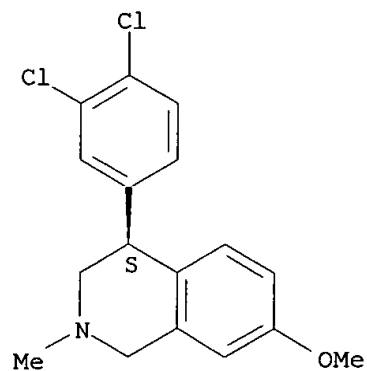


RE.CNT 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L48 ANSWER 5 OF 100 CAPLUS COPYRIGHT 2003 ACS  
 AN 1999:340074. CAPLUS  
 DN 131:125789  
 TI A cognate dopamine transporter-like activity endogenously expressed in a  
 COS-7 kidney-derived cell line  
 AU Sugamori, Kim S.; Lee, Frank J. S.; Pristupa, Zdenek B.; Niznik, Hyman B.  
 CS Department of Psychiatry, University of Toronto, Toronto, ON, Can.  
 SO FEBS Letters (1999), 451(2), 169-174  
 CODEN: FEBLAL; ISSN: 0014-5793  
 PB Elsevier Science B.V.  
 DT Journal  
 LA English  
 AB The activity of the dopamine transporter is an important mechanism for the  
 maintenance of normal dopaminergic homeostasis by rapidly removing  
 dopamine from the synaptic cleft. In kidney-derived COS-7, COS-1 and  
 HEK-293 but not in other mammalian cell lines (CHO, Y1, Ltk-), we have  
 characterized a putative functional dopamine transporter displaying a high  
 affinity (Km.apprx.250 nM) and a low capacity (.apprx.0.1 pmol/105  
 cells/min) for [3H]dopamine uptake. Uptake displayed a pharmacol. profile  
 clearly indicative of the neuronal dopamine transporter. Estd. Ki values  
 of numerous substrates and inhibitors for the COS-dopamine transporter and  
 the cloned human neuronal transporter (human dopamine transporter)  
 correlate well with the exception of a few notable compds., including the  
 endogenous neurotransmitter dopamine, the dopamine transporter inhibitor  
 GBR 12,909 and the dopaminergic agonist apomorphine. As with native  
 neuronal and cloned dopamine transporters, the uptake velocity was  
 sodium-sensitive and reduced by phorbol ester pre-treatment. Two mRNA  
 species of 3.8 and 4.0 kb in COS-7 cells were revealed by Northern blot  
 anal. similar in size to that seen in native neuronal tissue. A  
 reverse-transcribed PCR anal. confirmed the existence of a processed  
 dopamine transporter. However, no immunoreactive proteins of expected  
 dopamine transporter mol. size or [3H]WIN 35,428 binding activity were  
 detected. A partial cDNA of .apprx.1.3 kb, isolated from a COS-1 cDNA  
 library and encoding transmembrane domains 1-6, displayed a deduced amino  
 acid sequence homol. of .apprx.96% to the human dopamine transporter.  
 Taken together, the data suggest the existence of a non-neuronal  
 endogenous high affinity dopamine uptake system sharing strong functional  
 and mol. homol. to that of the cloned neuronal dopamine transporter.  
 IT 50560-38-8 50560-45-7  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological  
 process); BSU (Biological study, unclassified); BIOL (Biological study);  
 PROC (Process)  
 (pharmacol. profile of a cognate dopamine transporter-like activity  
 endogenously expressed in a COS-7 kidney-derived cell line)  
 RN 50560-38-8 CAPLUS  
 CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-  
 , (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

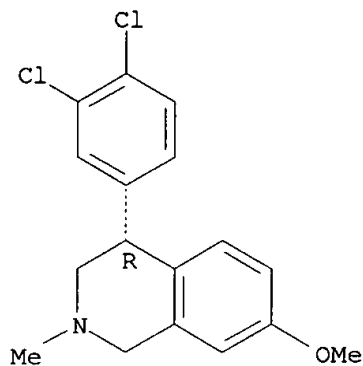




RN 50560-45-7 CAPLUS

CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-  
, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

148 ANSWER 6 OF 100 CAPLUS COPYRIGHT 2003 ACS

AN 1998:376413 CAPLUS

DN 129:4527

TI Additive and Vinylogous Pummerer Reactions of Amido Sulfoxides and Their Use in the Preparation of Nitrogen Containing Heterocycles

AU Padwa, Albert; Kuethe, Jeffrey T.

CS Department of Chemistry, Emory University, Atlanta, GA, 30322, USA

SO Journal of Organic Chemistry (1998), 63(13), 4256-4268

CODEN: JOCEAH; ISSN: 0022-3263

PB American Chemical Society

DT Journal

LA English

AB The .alpha.-thiocarbocation generated from the Pummerer reaction of 2-[4-MeC6H4S(:O)]C6H4CH2CONMe undergoes Friedel-Crafts reaction at the .gamma.-carbon with the tethered arom. ring. Reductive removal of the phenylthio group from the resulting product using Raney nickel occurs in high yield, and the overall reaction represents a new method for the synthesis of a variety of 3-phenyl-substituted oxindoles. Treatment of the related N-benzyl-N-alkyl amido sulfoxide system with trifluoroacetic anhydride affords tetrahydroisoquinoline derivs. The product distribution encountered coincides with the rotamer population of the starting amide. When the N-benzyl-N-Me amide is used, only the normal Pummerer product is formed. In this case, the thionium ion is generated in the wrong conformation for .pi.-cyclization to occur. The corresponding N-tert-Bu amido system, however, exists in a geometric orientation which places the benzylic group in the crucial conformation necessary for .pi.-cyclization, and consequently, the reaction proceeds smoothly. Related cyclization reactions occur in good yield with the corresponding furanyl and cyclohexenyl N-tert-Bu amido sulfoxides. The additive Pummerer reaction of 3-(phenylsulfinyl)-N-benzyl-N-tert-butylacrylamide gave products derived from both 5- and 6-exo trig cyclizations. Intramol. electrophilic arom. substitution via six-membered ring closure ultimately afforded a dihydropyridone. The competitive process involving ipso attack of the arom. ring on the thionium ion generates a spiro cyclohexadienyl cation that undergoes fragmentation of the adjacent .sigma.-bond. The resulting acyl iminium ion is converted to N-tert-butyl-2-phenyl-3-(phenylsulfinyl)acrylamide upon aq. workup. Only cyclizations leading to five-membered rings occur with the corresponding indolyl and alkenyl N-tert-Bu amido sulfoxides.

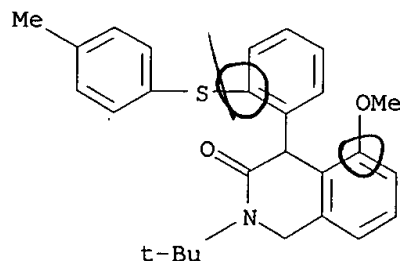
IT 207349-89-1P 207349-90-4P

RL: SPN (Synthetic preparation); PREP (Preparation)

(additive and vinylogous Pummerer reactions of amido sulfoxides in prepn. of nitrogen heterocycles)

RN 207349-89-1 CAPLUS

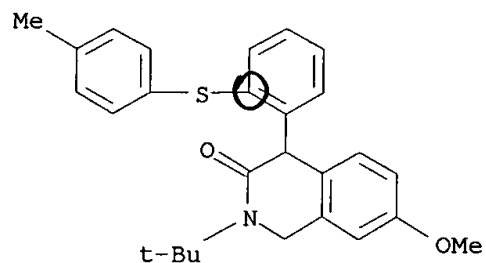
CN 3(2H)-Isoquinolinone, 2-(1,1-dimethylethyl)-1,4-dihydro-5-methoxy-4-[2-[(4-methylphenyl)thio]phenyl]- (9CI) (CA INDEX NAME)



09/704,306

RN 207349-90-4 CAPLUS

CN 3(2H)-Isoquinolinone, 2-(1,1-dimethylethyl)-1,4-dihydro-7-methoxy-4-[2-[(4-methylphenyl)thio]phenyl]- (9CI) (CA INDEX NAME)



RE.CNT 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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09/704,306

~~LA~~ ANSWER 7 OF 100 CAPLUS COPYRIGHT 2003 ACS  
~~AN~~ 1998:211847 CAPLUS  
DN 128:294669  
TI Synthesis of 7,12-dihydro-12-phenyl-5H-6,12-methanodibenz[c,f]azocines via  
N,N-dibenzylphenacylamines  
AU Coskun, Necdet; Buyukuysal, Levent  
CS Dep. Chem., Uludag Univ., Bursa, 16059, Turk.  
SO Heterocycles (1998), 48(1), 53-59  
CODEN: HTCYAM; ISSN: 0385-5414  
PB Japan Institute of Heterocyclic Chemistry  
DT Journal  
LA English  
GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB N,N-Dibenzylphenacylamines I (R1 = R2 = MeO, R3 = R4 = R5 = R6 = H; R1 = R6 = H, R2 = R3 = R4 = R5 = MeO; R1R2 = OCH2O, R3 = R6 = H, R4 = R5 = MeO; etc.) were prepd. in high yields by a one-pot reaction and cyclized at room temp. to give 7,12-dihydro-12-phenyl-5H-6,12-methanodibenz[c,f]azocines II in high yields. 95% H2SO4 or 70% HClO4 was used as cyclization catalysts. The double-cyclization proceeds smoothly in the cases where electron-donating groups are present in both benzene rings. N-2,3-dimethoxybenzyl-N-benzylphenacylamine gave the corresponding N-benzyl-1,2-dihydro-4-phenylisoquinoline on treatment with 95% H2SO4 while N-3,4-dimethoxybenzyl-N-benzylphenacylamine at the same reaction conditions and reaction time cyclized to the corresponding dibenzazocine. However, N-3,4-dimethoxybenzyl-N-benzylphenacylamine gave the corresponding dihydroisoquinoline which disproportionates to give N-benzyl-1,2,3,4-tetrahydro-4-phenylisoquinoline and N-benzyl-4-phenylisoquinolinium when treated with 70% perchloric acid at room temp.

IT 206126-07-0P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of phenylmethanodibenzazocines by cyclization of  
dibenzylphenacylamines)

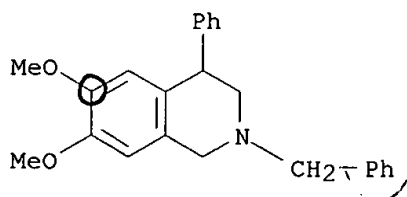
RN 206126-07-0 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-6,7-dimethoxy-4-phenyl-2-(phenylmethyl)-,  
perchlorate (9CI) (CA INDEX NAME)

CM 1

CRN 206126-06-9

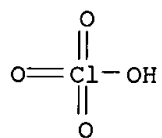
CMF C24 H25 N O2



CM 2

09/704,306

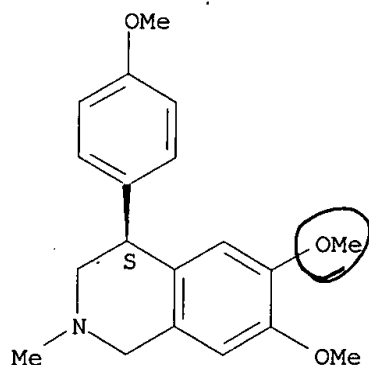
CRN 7601-90-3  
CMF Cl H O4



09/704,306

~~LA8~~ ANSWER 8 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1998:85154 CAPLUS  
DN 128:167138  
TI Chiroptical properties and absolute configuration of pyrroloisoquinoline antidepressants  
AU Maryanoff, Bruce E.; McComsey, David F.; Craig, J. Cymerman  
CS Drug Discovery, The R. W. Johnson Pharmaceutical Research Institute, PA, 19477, USA  
SO Chirality (1998), 10(1/2), 169-172  
CODEN: CHRLEP; ISSN: 0899-0042  
PB Wiley-Liss, Inc.  
DT Journal  
LA English  
AB CD (CD) spectra were detd. for the bioactive (+)-enantiomers of 1 .cntdot. HCl, 3 .cntdot. HCl, and 4 .cntdot. HBr to characterize the chiroptical properties of these pyrroloisoquinoline antidepressants. The compds. showed a low-intensity neg. CD band with much fine structure between 252 and 272 nm, a medium neg. CD band with fine structure between 215 and 225 nm, and a high-intensity neg. CD max. between 198 and 203 nm. Except for amplitude variation, the three CD spectra were essentially superimposable in sign and position of the bands. The CD curves for the (-)-enantiomers of 1 .cntdot. HCl and 4 .cntdot. HBr were opposite in sign and comparable within 5% to the (+)-enantiomers. The results are consistent with the previously assigned (Maryanoff et al. J. Med. Chem. 30:1433-1454, 1987) abs. configurations of (6S, 10bR) for 1 and 3, and (6R, 10bR) for 4.  
IT 23367-60-4  
RL: ARU (Analytical role, unclassified); PRP (Properties); ANST (Analytical study)  
(chiroptical properties and abs. configuration of pyrroloisoquinoline)  
RN 23367-60-4 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-6,7-dimethoxy-4-(4-methoxyphenyl)-2-methyl-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L48 ANSWER 9 OF 100 CAPLUS COPYRIGHT 2003 ACS

AN 1998:53462 CAPLUS

DN 128:200880

TI .gamma.-aminobutyric acidA agonists differentially augment gnawing induced by indirect-acting dopamine agonists in C57BL/6J mice

AU Tirelli, Ezio; Geter-Douglass, Beth; Witkin, Jeffrey M.

CS Drug Development Group, Preclinical Pharmacology Laboratory, Addiction Research Center, National Institute on Drug Abuse, National Institutes of Health, Baltimore, MD, USA

SO Journal of Pharmacology and Experimental Therapeutics (1998), 284(1), 116-124

CODEN: JPETAB; ISSN: 0022-3565

PB Williams &amp; Wilkins

DT Journal

LA English

AB Evidence from structure-activity, mol. biol., ligand binding and behavioral studies has suggested potential differences in the pharmacol. effects of indirect dopamine agonists. Striatal dopaminergic neurotransmission is under the regulatory control of GABAergic inputs. The ability of agonists of .gamma.-aminobutyric acidA (GABAA) receptors to enhance stereo-typed gnawing was used as a method for dissocg. the pharmacol. effects of indirect-acting dopamine agonists. Gnawing on corrugated cardboard was studied in C57BL/6J mice. The GABAA agonists, gaboxadol HCl (THIP) and muscimol, were not effective in augmenting gnawing in the presence of the direct-acting dopamine agonists, apomorphine, pergolide, RU 24213 or SKF 38393. In addn., THIP did not enhance the gnawing produced by cocaine, bupropion, GBR 12909 or WIN 35428. In contrast, THIP produced marked augmentation of the gnawing induced by methylphenidate, (+)-amphetamine, methamphetamine, amfonelic acid, indatraline, nomifensine, diclofensine, mazindol and GBR 12935. The qual. differences in potentiation were not caused by differences in the maximal effect of the drugs alone, inadequate dose or routes of administration, or by differences in duration of action. Neither can the absence of potentiation be accounted for by unique effects of THIP; muscimol was only marginally effective in potentiating the effects of WIN 35428 and bupropion but completely inactive in augmenting the effects of cocaine and GBR 12909. Muscimol was efficacious in augmenting the effects of the drugs for which THIP was active. These results add to a small but growing literature that demonstrates differences in the in vitro and in vivo pharmacol. effects of indirect dopamine agonists. The methods used here may help in defining the mol. and neural substrates of these differential effects.

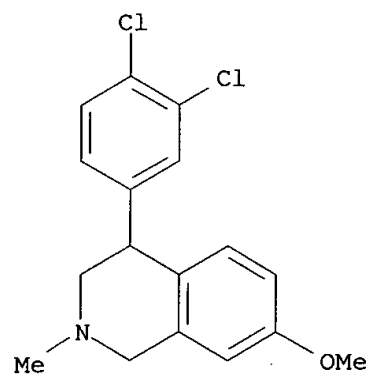
IT 67165-56-4, Diclofensine

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(differential discrimination of indirect-acting dopamine agonists)

RN 67165-56-4 CAPLUS

CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl- (9CI) (CA INDEX NAME)





~~1~~8 ANSWER 10 OF 100 CAPLUS COPYRIGHT 2003 ACS

~~UN~~ 1996:644882 CAPLUS

~~DN~~ 125:292276

TI 4-(3,4-Dihydroxyphenyl)-1,2,3,4-tetrahydroisoquinoline derivatives. II.  
Their renal vasodilation activity and structure-activity relationship

AU Anan, Hideki; Tanaka, Akihiro; Tsuzuki, Ryuji; Yokota, Masaki; Yatsu,  
Takeyuki; Fujikura, Takashi

CS Inst. Drug Discovery Res., Yamanouchi Pharmaceutical Co., Ltd., Ibaraki,  
305, Japan

SO Chemical & Pharmaceutical Bulletin (1996), 44(10), 1865-1870

CODEN: CPBTAL; ISSN: 0009-2363

PB Pharmaceutical Society of Japan

DT Journal

LA English

AB A series of 4-(3,4-dihydroxyphenyl)-1,2,3,4-tetrahydroisoquinoline derivs.  
showed potent DA1 agonistic activities. We investigated the  
structure-activity relation of the racemic compds. of this series.  
4-(3,4-Dihydroxyphenyl)-7-methanesulfonamido-1,2,3,4-  
tetrahydroisoquinoline (43) was identified as a potent renal vasodilator  
with activity almost equal to that of YM435 (1).

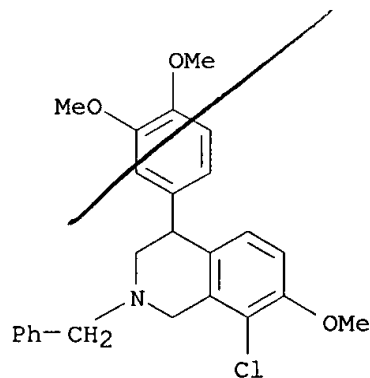
IT 119085-55-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic  
preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant  
or reagent)

(dihydroxyphenyl)tetrahydroisoquinoline derivs. and their renal  
vasodilation activity and structure-activity relationship)

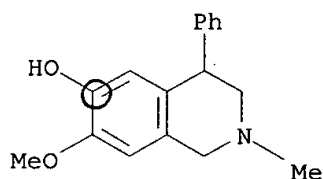
RN 119085-55-1 CAPLUS

CN Isoquinoline, 8-chloro-4-(3,4-dimethoxyphenyl)-1,2,3,4-tetrahydro-7-  
methoxy-2-(phenylmethyl)- (9CI) (CA INDEX NAME)

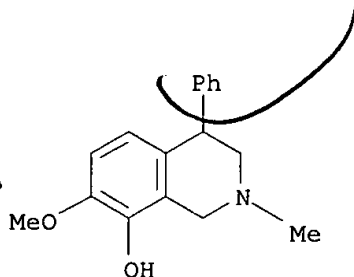


09/704,306

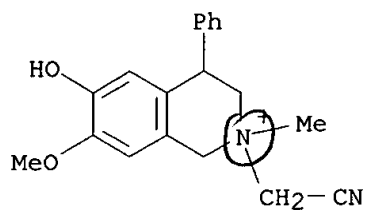
~~LA~~ 8 ANSWER 11 OF 100 CAPLUS COPYRIGHT 2003 ACS  
~~AN~~ 1995:807701 CAPLUS  
DN 123:314219  
TI A novel ring cleavage and recyclization of N-cyanomethyl-1,2,3,4-tetrahydroisoquinolinium methiodides: a biomimetic synthesis of litebamine  
AU Hara, Hiroshi; Kaneko, Ken-ichi; Endoh, Masaki; Uchida, Hideharu; Hoshino, Osamu  
CS Fac. Pharm. Sci., Sci. Univ. Tokyo, Tokyo, 162, Japan  
SO Tetrahedron (1995), 51(37), 10189-204  
CODEN: TETRAB; ISSN: 0040-4020  
PB Elsevier  
DT Journal  
LA English  
AB Treatment of N-cyanomethyl-6-hydroxy-1,2,3,4-tetrahydroisoquinolinium methiodide with NaOMe in MeOH caused C(1)-N fission and simultaneous recyclization to give 8-hydroxy-5-methoxymethyl-1,2,3,4-tetrahydroisoquinoline. This rearrangement was used in the synthesis of litebamine.  
IT 88776-67-4 88776-68-5  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(ring cleavage and recyclization of cyanomethyltetrahydroisoquinolinium methiodides and biomimetic synthesis of litebamine)  
RN 88776-67-4 CAPLUS  
CN 6-Isoquinolinol, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-phenyl- (9CI)  
(CA INDEX NAME)



RN 88776-68-5 CAPLUS  
CN 8-Isoquinolinol, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-phenyl- (9CI)  
(CA INDEX NAME)



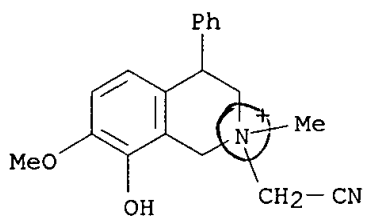
IT 147734-10-9P 147734-14-3P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(ring cleavage and recyclization of cyanomethyltetrahydroisoquinolinium methiodides and biomimetic synthesis of litebamine)  
RN 147734-10-9 CAPLUS  
CN Isoquinolinium, 2-(cyanomethyl)-1,2,3,4-tetrahydro-6-hydroxy-7-methoxy-2-methyl-4-phenyl-, iodide (9CI) (CA INDEX NAME)



● I<sup>-</sup>

RN 147734-14-3 CAPLUS

CN Isoquinolinium, 2-(cyanomethyl)-1,2,3,4-tetrahydro-8-hydroxy-7-methoxy-2-methyl-4-phenyl-, iodide (9CI) (CA INDEX NAME)



● I<sup>-</sup>

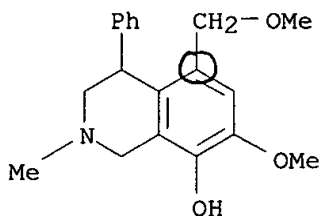
IT 169900-81-6P 169900-85-0P 169901-01-3P

169901-02-4P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(ring cleavage and recyclization of cyanomethyltetrahydroisoquinolinium methiodides and biomimetic synthesis of litebamine)

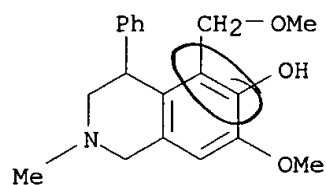
RN 169900-81-6 CAPLUS

CN 8-Isoquinolinol, 1,2,3,4-tetrahydro-7-methoxy-5-(methoxymethyl)-2-methyl-4-phenyl- (9CI) (CA INDEX NAME)



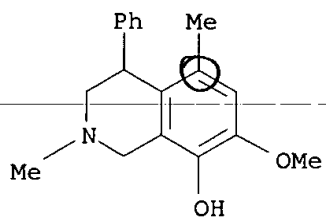
RN 169900-85-0 CAPLUS

CN 6-Isoquinolinol, 1,2,3,4-tetrahydro-7-methoxy-5-(methoxymethyl)-2-methyl-4-phenyl- (9CI) (CA INDEX NAME)



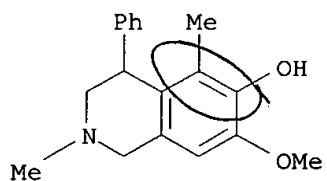
RN 169901-01-3 CAPLUS

CN 8-Isoquinolinol, 1,2,3,4-tetrahydro-7-methoxy-2,5-dimethyl-4-phenyl- (9CI)  
(CA INDEX NAME)

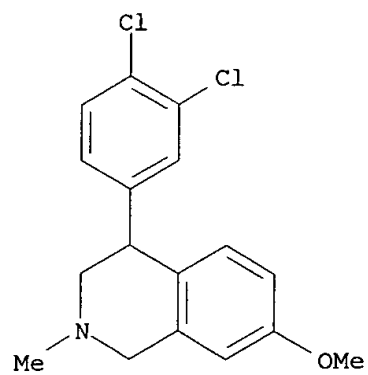


RN 169901-02-4 CAPLUS

CN 6-Isoquinolinol, 1,2,3,4-tetrahydro-7-methoxy-2,5-dimethyl-4-phenyl- (9CI)  
(CA INDEX NAME)



L48 ANSWER 12 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1995:739229 CAPLUS  
DN 123:188282  
TI Effects of various dopamine uptake inhibitors on striatal extracellular dopamine levels and behaviors in rats  
AU Nakachi, Noriyuki; Kiuchi, Yuji; Inagaki, Masahiro; Inazu, Masato; Yamazaki, Yukako; Oguchi, Katsuji  
CS Department of Pharmacology, School of Medicine, Showa University, 1-5-8 Hatanodai, Shinagawa-ku, Tokyo, 142, Japan  
SO European Journal of Pharmacology (1995), 281(2), 195-203  
CODEN: EJPHAZ; ISSN: 0014-2999  
PB Elsevier  
DT Journal  
LA English  
AB In vivo central effects of some dopamine uptake inhibitors were evaluated in both brain microdialysis and behavioral studies in rats, and compared with their in vitro affinities to dopamine uptake sites. IC50 values of GBR12909 (1-[2-[bis(4-fluorophenyl)methoxy]ethyl]-4-(3-phenylpropyl)piperazine), diclofensine, mazindol, amfonelic acid and nomifensine for inhibiting 1 nM [<sup>3</sup>H]GBR12935 (1-[2-(diphenylmethoxy)ethyl]-4-(3-phenylpropyl)piperazine) binding to rat striatal membrane were 7.0, 36, 81, 187 and 290 nM, resp. In the brain microdialysis study, dopamine levels in the striatal dialyzates were increased to 16.3- (GBR12909), 14.1- (nomifensine), 4.8- (diclofensine) and 1.9-fold (amfonelic acid) above the resp. basal levels 40-60 min after i.p. administration (0.1 mmol/kg) and thereafter the dopamine levels decreased slowly but remained elevated for a further 3 h, while mazindol gradually increased dopamine levels less than did the other agents (1.7-fold 200 min after administration). Remarkable and comparable stereotyped behaviors (licking and forepaw treading) were continuously obsd. for at least 3 h after administration of GBR12909, nomifensine and amfonelic acid, while stereotypies induced by diclofensine and mazindol were moderate and marginal, resp. In vivo potencies of dopamine uptake inhibitors to increase the extracellular dopamine levels in the striatum tended to correlate with their in vitro affinities to dopamine uptake sites except for nomifensine, and correlated significantly with their potencies to induce stereotyped behaviors except for amfonelic acid. Based on these findings, pharmacol. characteristics of these dopamine uptake inhibitors are discussed.  
IT 67165-56-4, Diclofensine  
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(effects of various dopamine uptake inhibitors on striatal extracellular dopamine levels and stereotyped behavior in rats in relation to binding of dopamine uptake sites)  
RN 67165-56-4 CAPLUS  
CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl- (9CI) (CA INDEX NAME)



L48 ANSWER 13 OF 100 CAPLUS COPYRIGHT 2003 ACS

AN 1995:714876 CAPLUS

DN 123:131868

TI Determination of a cardiac antiarrhythmic, tricyclic antipsychotics and antidepressants in human and animal urine by micellar electrokinetic capillary chromatography using a bile salt

AU Aumatell, Anthony; Wells, Robert J.

CS Australian Government Analytical Laboratory, 1 Suakin Street, Pymble, NSW, 2073, Australia

SO Journal of Chromatography, B: Biomedical Applications (1995), 669(2), 331-44

CODEN: JCBBEF; ISSN: 0378-4347

PB Elsevier

DT Journal

LA English

AB A micellar electrokinetic capillary chromatog. method based on the use of sodium taurodeoxycholate has been developed to detect and quantitate a total of 26 tricyclic drugs. Detection limits in urine down to 4 ng/mL have been obtained. The method uses a simple liq.-liq. extn. and recovery of analytes followed by UV detection.

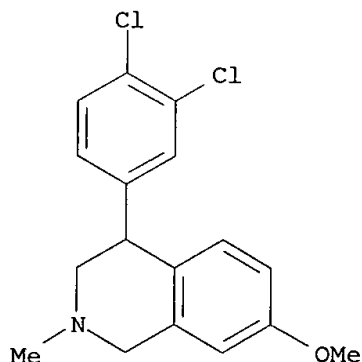
IT 67165-56-4, Diclofensine

RL: ANT (Analyte); ANST (Analytical study)

(cardiac antiarrhythmic, tricyclic antipsychotic, and antidepressant detn. in human and animal urine by micellar electrokinetic capillary chromatog. using a bile salt)

RN 67165-56-4 CAPLUS

CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-(9CI) (CA INDEX NAME)



148 ANSWER 14 OF 100 CAPLUS COPYRIGHT 2003 ACS

AN 1995:704598 CAPLUS

DN 123:313715

TI Synthesis and .kappa. binding affinity of 1-(pyrrolidin-1-ylmethyl)-2-(N-methyl)-4-[(3,4-dichlorophenyl)-1,2,3,4-tetrahydroisoquinolin-3(2H)-ones

AU Pinna, G. A.; Gavini, E.; Cignarella, G.; Scolastico, S.; Fadda, P.

CS Istituto Chimia Farmaceutica, Sassari, 07100, Italy

SO European Journal of Medicinal Chemistry (1995), 30(6), 515-20

CODEN: EJMCA5; ISSN: 0223-5234

PB Elsevier

DT Journal

LA English

AB Diastereomeric forms of 1-(pyrrolidin-1-ylmethyl)-2-(N-methyl)-4-[(3,4-dichlorophenyl)-1,2,3,4-tetrahydroisoquinolin-3(2H)-ones (3a) and its chloro analog (3c) were synthesized. Compds. 3a,c are related to the .kappa.-selective opiate ICI 199441 (1). Compared with morphine, these compds. had lower .kappa. and .mu. affinities; only cis-3a showed a modest .kappa. affinity. 1-Pyrrolidin-1-ylmethyl-N-[2-(3,4-dichlorophenyl)acetyl]-1,2,3,4-tetrahydroisoquinoline (2), which is also a cyclic congener of 1, was reported to display high .kappa. and .mu. affinity, and so a conformational study was undertaken on 1, 2 and 3a. This showed that, while active 2 extensively superposed on 1, 3a assumes another geometry which does not allow a fit with the pharmacophoric moieties of 1 and 2.

IT 170119-28-5P 170119-29-6P 170119-30-9P

170119-31-0P

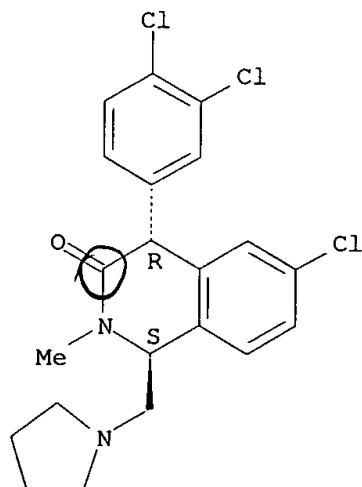
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(synthesis and .kappa. binding affinity of  
(pyrrolidinylmethyl)(dichlorophenyl)tetrahydroisoquinolinones)

RN 170119-28-5 CAPLUS

CN 3(2H)-Isoquinolinone, 6-chloro-4-(3,4-dichlorophenyl)-1,4-dihydro-2-methyl-1-(1-pyrrolidinylmethyl)-, (1S-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 170119-29-6 CAPLUS

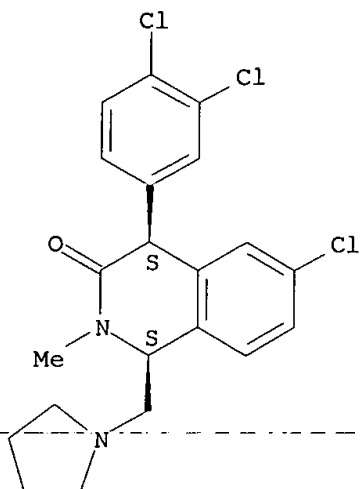
CN 3(2H)-Isoquinolinone, 6-chloro-4-(3,4-dichlorophenyl)-1,4-dihydro-2-methyl-



09/704,306

1-(1-pyrrolidinymethyl)-, (1S-cis)- (9CI) (CA INDEX NAME)

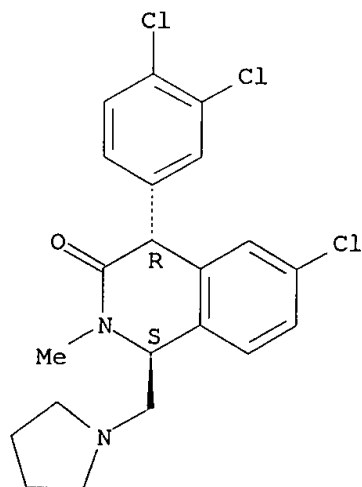
Absolute stereochemistry.



RN 170119-30-9 CAPLUS

CN 3(2H)-Isoquinolinone, 6-chloro-4-(3,4-dichlorophenyl)-1,4-dihydro-2-methyl-1-(1-pyrrolidinymethyl)-, monohydrochloride, (1S-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

RN 170119-31-0 CAPLUS

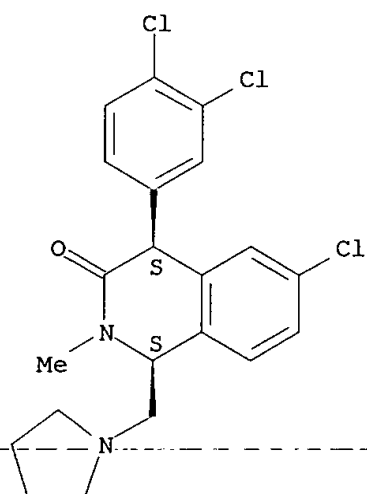
CN 3(2H)-Isoquinolinone, 6-chloro-4-(3,4-dichlorophenyl)-1,4-dihydro-2-methyl-1-(1-pyrrolidinymethyl)-, monohydrochloride, (1S-cis)- (9CI) (CA INDEX NAME)

Brenda Coleman

<page

09/704,306

Absolute stereochemistry.



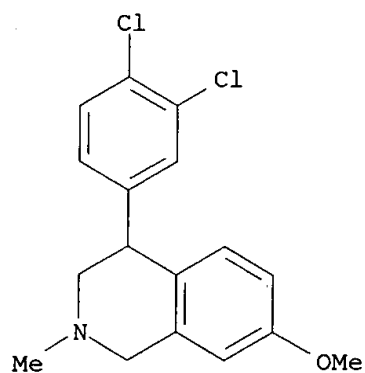
● HCl

L48 ANSWER 15 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1995:505643 CAPLUS  
DN 122:282072  
TI Differential effects of direct and indirect dopamine agonists on the induction of gnawing in C57BI/6J mice  
AU Tirelli, Ezio; Witkin, Jeffrey M.  
CS Psychobiology Section, National Institute on Drug Abuse Addiction Research Center, Baltimore, MD, USA  
SO Journal of Pharmacology and Experimental Therapeutics (1995), 273(1), 7-15  
CODEN: JPETAB; ISSN: 0022-3565  
PB Williams & Wilkins  
DT Journal  
LA English  
AB The ability of indirect dopamine agonists to induce gnawing in male C57BI/6J mice was compared to that of direct dopamine agonists acting at dopamine D1 or D2 receptor subtypes. Holes left by the mice on the corrugations of packing cardboard were used as an objective index of gnawing. Indirect dopamine agonists, including dopamine releasers such as fencamfamine, (+)-amphetamine and amfonelic acid and dopamine uptake inhibitors such as cocaine, GBR 12909 [1-[2-[bis(4-fluorophenyl)methoxy]ethyl]-4-[3-phenylpropyl]piperazine diHCl} and nomifensine produced dose-dependent increases in gnawing. None of the direct agonists (e.g., apomorphine, quinpirole or SKF 82958 [(+)-6-chloro-7,8-dihydroxy-3-allyl-1-phenyl-2,3,4,5-tetrahydro-1H-3-benzazepine]) increased gnawing. Although these compds. varied in potency and efficacy, 18 structurally diverse compds. induced gnawing in 100% of the mice tested. Four weak indirect agonists (3,4-methylenedioxymethamphetamine, amantadine, 2-phenylethylamine and benztropine) failed to induce gnawing. The lack of efficacy of postsynaptic dopamine agonists was not changed by various combinations of postsynaptic agonists (e.g., dopamine D1 and D2 agonists in combination). Nonetheless, the dopaminergic nature of the gnawing response was confirmed in expts. in which a host of compds. with primary actions at non-dopaminergic sites did not induce gnawing; compds. included nicotine, caffeine, dizocilpine, lidocaine, fluoxetine and nisoxetine. In addn., both the dopamine D1 antagonist SCH 23390 [R-(+)-7-chloro-8-hydroxy-3-methyl-1-phenyl-2,3,4,5-tetrahydro-1H-3-benzazepine], the D2 antagonist eticlopride and the dopamine D1/D2 antagonist flupenthixol produced dose-dependent blockade of gnawing induced by either cocaine or methylphenidate. All of the antagonists blocked gnawing at doses below those producing decreases in spontaneous locomotor activity, with eticlopride showing the greatest selectivity in blocking gnawing over locomotor suppression (7- to 14-fold). Given the general contrast between the effects of direct and indirect dopamine agonists, the present procedure could serve as a rapid in vivo method of distinguishing direct- from indirect-acting dopamine agonists.

IT **34041-84-4**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(differential effects of direct and indirect dopamine agonists on the induction of gnawing in C57BI/6J mice)

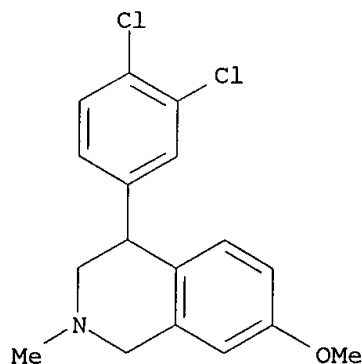
RN 34041-84-4 CAPLUS  
CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-, hydrochloride (8CI, 9CI) (CA INDEX NAME)

09/704,306



● HCl

L48 ANSWER 16 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1995:320795 CAPLUS  
DN 122:170347  
TI Enantiomeric differentiation of a wide range of pharmacologically active substances by cyclodextrin-modified micellar electrokinetic capillary chromatography using a bile salt  
AU Aumatell, Anthony; Wells, Robert J.  
CS Australian Government Analytical Laboratory, 1 Suakin Street, Pymble, NSW, 2073, Australia  
SO Journal of Chromatography, A (1994), 688(1 + 2), 329-37  
CODEN: JCRAEY; ISSN: 0021-9673  
PB Elsevier  
DT Journal  
LA English  
AB This paper shows the versatility of modified charged and non-charged .beta.-cyclodextrins in micellar systems for optically resolving .beta.-agonists, .beta.-antagonists, phenylethylamines stimulants and diclofensine an antidepressant. A total of 22 compds. were optically resolved using hydroxypropyl-.beta.-cyclodextrin with sodium taurodeoxycholate and sodium sulfobutyl ether-.beta.-cyclodextrin with sodium dodecyl sulfate.  
IT **67165-56-4P**, Diclofensine  
RL: ANT (Analyte); PUR (Purification or recovery); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(enantiomeric differentiation of a wide range of drugs by cyclodextrin-modified micellar electrokinetic capillary chromatog. using a bile salt)  
RN 67165-56-4 CAPLUS  
CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-(9CI) (CA INDEX NAME)



L48 ANSWER 17 OF 100 CAPLUS COPYRIGHT 2003 ACS

AN 1995:221528 CAPLUS

DN 122:305842

TI Reversal of multidrug resistance by bis(phenylalkyl)amines and structurally related compounds

AU Ramu, Avner; Ramu, Nili

CS Department Oncology, Hadassah University Hospital, Jerusalem, 91120, Israel

SO Cancer Chemotherapy and Pharmacology (1994), 34(5), 423-30

CODEN: CCPHDZ; ISSN: 0344-5704

DT Journal

LA English

AB We have previously reported that multidrug (MDR)-reversal activity can be exerted by compds. in which two ring structures of certain types are connected by one alkyl bridge to a secondary or tertiary amine group. In the present investigation we studied the MDR-reversal activity of compds. in which the two ring structure were connected by sep. alkyl bridges to the amine group. The structure-activity relationship of these compds. verified previous findings on the structural features that support MDR-reversal activity as well as the features that reduce such activity. In addn., the present study reveals addnl. chem. groups and ring structures that support MDR-reversal activity as well as those that reduce it.

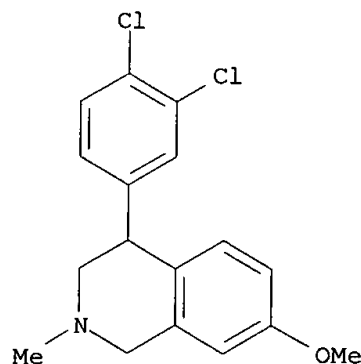
IT **67165-56-4**, Diclofensine

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

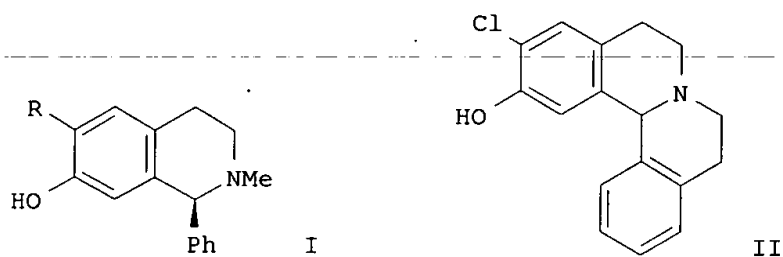
(multidrug resistance reversal by bis(phenylalkyl)amines and structurally related compds.)

RN 67165-56-4 CAPLUS

CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-(9CI) (CA INDEX NAME)



✓  
 148 ANSWER 18 OF 100 CAPLUS COPYRIGHT 2003 ACS  
 AN 1995:192226 CAPLUS  
 DN 122:9840  
 TI Synthesis and Molecular Modeling of 1-Phenyl-1,2,3,4-tetrahydroisoquinolines and Related 5,6,8,9-Tetrahydro-13bH-dibenzo[a,h]quinolizines as D1 Dopamine Antagonists  
 AU Minor, Deborah L.; Wyrick, Steven D.; Charifson, Paul S.; Watts, Val J.; Nichols, David E.; Mailman, Richard B.  
 CS School of Pharmacy, University of North Carolina, Chapel Hill, NC, 27599-7360, USA  
 SO Journal of Medicinal Chemistry (1994), 37(25), 4317-28  
 CODEN: JMCMAR; ISSN: 0022-2623  
 DT Journal  
 LA English  
 GI



AB New 1-phenyl-1,2,3,4-tetrahydroisoquinolines and related 5,6,8,9-tetrahydro-13bH-dibenzo[a,h]quinolizines were prep'd. as ring-contracted analogs of the prototypical 1-phenyl-2,3,4,5-tetrahydrobenzazepines (e.g., SCH23390) as a continuation of our studies to characterize the antagonist binding pharmacophore of the D1 dopamine receptor. Receptor affinity was assessed by competition for [<sup>3</sup>H]SCH23390 binding sites in rat striatal membranes. The 6-bromo-1-phenyltetrahydroisoquinoline analog I (R = Br) of SCH23390 had D1 binding affinity similar to that for the previously reported 6-chloro analog I (R = Cl), whereas the 6,7-dihydroxy analog had significantly lower D1 affinity. Conversely, neither 6-monohydroxy- nor 7-monohydroxy-1-phenyltetrahydroisoquinolines had significant affinity for the D1 receptor. These results demonstrate that 6-halo and 7-hydroxy substituents influence D1 binding affinity of the 1-phenyltetrahydroisoquinolines in a fashion similar to their effects on 1-phenyltetrahydrobenzazepines. The conformationally constrained 3-chloro-2-hydroxytetrahydrodibenzoquinolizine II had much lower affinity relative to the corresponding, and more flexible, 6-chloro-7-hydroxy-1-phenyltetrahydroisoquinoline I (R = Cl). Similarly, the 2,3-dihydroxytetrahydrodibenzoquinolizine had much lower D1 affinity compared to dihydrexidine, a structurally similar hexahydrobenzo[a]phenanthridine that is a high-affinity full D1 agonist. Together, these data not only confirm the effects of the halo and hydroxy substituents on the parent nucleus but demonstrate the pharmacophoric importance of both the nitrogen position and the orientation of the accessory Ph ring in modulating D1 receptor affinity and function. Mol. modeling studies and conformational analyses were conducted using the data from these new analogs in combination with the data from compds. previously synthesized. The resulting geometries were used to refine a

working model of the D1 antagonist pharmacophore using conventional quant. structure-activity relationships and three-dimensional QSAR (CoMFA).

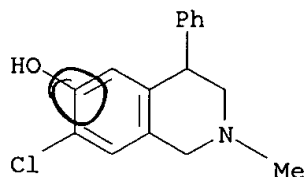
IT **115514-82-4**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(synthesis and mol. modeling of phenyltetrahydroisoquinolines and related tetrahydrodibenzoquinolizines as D1 dopamine antagonists)

RN 115514-82-4 CAPLUS

CN 6-Isoquinolinol, 7-chloro-1,2,3,4-tetrahydro-2-methyl-4-phenyl- (9CI) (CA INDEX NAME)





L48 ANSWER 19 OF 100 CAPLUS COPYRIGHT 2003 ACS

AN 1994:645160 CAPLUS

DN 121:245160

TI Differential relationships among dopamine transporter affinities and stimulant potencies of various uptake inhibitors

AU Izenwasser, Sari; Terry, Philip; Heller, Brett; Witkin, Jeffrey M.; Katz, Jonathan L.

CS Psychobiology Section, National Institute on Drug Abuse, Intramural Research Program, National Institutes of Health, P.O. Box 5180, Baltimore, MD, 21224, USA

SO European Journal of Pharmacology (1994), 263(3), 277-83  
CODEN: EJPHAZ; ISSN: 0014-2999

DT Journal

LA English

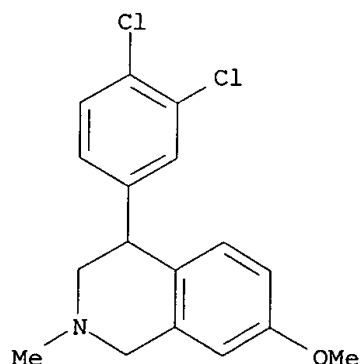
AB Binding to the dopamine transporter and inhibiting dopamine reuptake are considered important factors in regulating behavioral effects of cocaine. One prominent behavioral effect of cocaine and other dopamine uptake inhibitors is the stimulation of locomotor activity. To examine the relationship between action at the dopamine transporter and behavior, the displacement of  $[^3\text{H}]\text{WIN-35,428}$  (CFT naphthalene sulfate; 2-.beta.-carbomethoxy-3-.beta.-(4-fluorophenyl)tropane-1,5-naphthalene disulfonate) binding in rat caudate putamen by cocaine and other uptake inhibitors was compared with stimulation of mouse locomotor activity. There was a significant correlation among affinities for binding and potencies for stimulating activity for cocaine and structurally similar compds. For structurally dissimilar uptake inhibitors, however, there was no significant correlation among potencies for stimulation of activity and affinity for displacement of  $[^3\text{H}]\text{WIN-35,428}$  binding. These findings provide evidence that cocaine analogs may bind to the dopamine transporter in a manner that is fundamentally different from that for structurally dissimilar uptake inhibitors.

IT 67165-56-4, Diclofensine

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(differential relationships among dopamine transporter affinities and stimulant potencies of various uptake inhibitors)

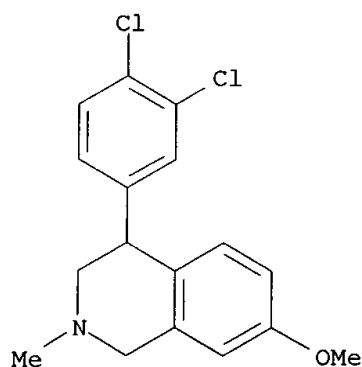
RN 67165-56-4 CAPLUS

CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-(9CI) (CA INDEX NAME)



L48 ANSWER 20 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1994:473613 CAPLUS  
DN 121:73613  
TI Effects of various dopamine uptake inhibitors on behaviors and striatal dopaminergic system in rats  
AU Nakachi, Noriyuki; Kiuchi, Yuji; Inagaki, Masahiro; Inazu, Masato; Morioka, Daichi; Yamazaki, Yukako; Kanda, Yuko; Yokomizo, Chie; Oguchi, Katsuji  
CS Sch. Med., Showa Univ., Tokyo, Japan  
SO Yakubutsu, Seishin, Kodo (1992), 12(6), 308  
CODEN: YSKODB; ISSN: 0285-5313  
DT Journal  
LA Japanese  
AB The effects of 5 dopamine uptake inhibitors, GBR 12909, amfonelic acid, nomifensine, diclofensine, and mazindol, on striatal dopamine metab. were correlated with locomotor and stereotyped behaviors in rats following i.p. administration of the above drugs.  
IT **67165-56-4**, Diclofensine  
RL: BIOL (Biological study)  
RN 67165-56-4 CAPLUS  
CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-(9CI) (CA INDEX NAME)

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L48 ANSWER 21 OF 100 CAPLUS COPYRIGHT 2003 ACS

AN 1994:449612 CAPLUS

DN 121:49612

TI A new pharmacophoric model for 5-HT reuptake-inhibitors: differentiation of amphetamine analogs

AU Rupp, Armin; Kovar, Karl-Artur; Beuerle, Gerald; Ruf, Claus; Folkers, Gerd  
CS Pharmazeutisches Institut der Universitaet Tuebingen, Auf der Morgenstelle 8, 72076, Tübingen, Germany

SO Pharm. Acta Helv. (1994), 68(4), 235-44

CODEN: PAHEAA; ISSN: 0031-6865

DT Journal

LA English

AB A pharmacophoric model for 5-HT reuptake-inhibitors was developed using the pharmacophore elements geometry and MEP (Mol. Electrostatic Potential) by the method of active analog approach. This model is characterized by: (1) a protonated basic nitrogen sep'd. by 610 pm from the center of an arom. system and 920 pm from an electroneg. substituent of this arom. system, (2) a region with n- and/or .pi.-electrons along the axis substituent-arom. system-nitrogen atom, (3) an aliph. side chain which joins the region of the n- and/or .pi.-electrons with the nitrogen atom, (4) an addnl. arom. group at right angles to the pharmacophoric arom. group below the protonated nitrogen and (5) a forbidden region on the pharmacophore which leads to a deviation of the allowed tubular orientation of the ligand. The pharmacophore model enables a differentiation of the entactogenic, hallucinogenic and stimulating arylalkanamines. The theor. considerations are confirmed by a postulated intramol. H-bonding in the active conformation of the selective 5-HT reuptake-inhibitor, citalopram, which could be proved by NMR- and IR-spectroscopic measurements.

IT 50560-38-8

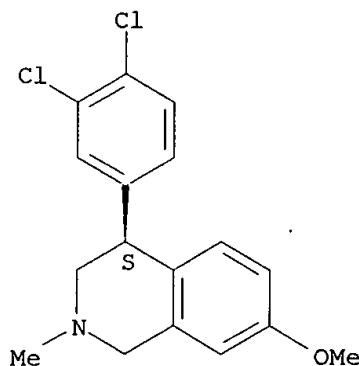
RL: BIOL (Biological study)

(serotonin reuptake inhibition by, pharmacophoric model for differentiation of amphetamine analogs in relation to)

RN 50560-38-8 CAPLUS

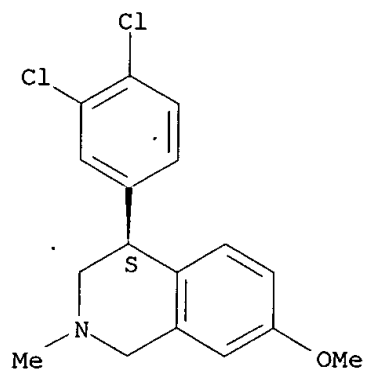
CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L48 ANSWER 22 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1994:153599 CAPLUS  
DN 120:153599  
TI Pharmacological heterogeneity of the cloned and native human dopamine transporter: disassociation of [3H]WIN 35,428 and [3H]GBR 12,935 binding  
AU Pristupa, Zdenek B.; Wilson, Julie M.; Hoffman, Beth J.; Kish, Stephen J.; Niznik, Hyman B.  
CS Dep. Psychiatry, Univ. Toronto, Bethesda, MD, USA  
SO Molecular Pharmacology (1994), 45(1), 125-35  
CODEN: MOPMA3; ISSN: 0026-895X  
DT Journal  
LA English  
AB Controversy exists as to whether the functional state of the dopamine (DA) transporter is identical to sites mediating the specific binding of selective DA transporter radioligands. Therefore, the authors compared the pharmacol. profile of numerous dopamine transport substrates and inhibitors on [3H]DA uptake with the binding of [3H]WIN 35,428 and [3H]GBR 12,935 to COS-7 cells transiently expressing the cloned human DA transporter. [3H]DA uptake and [3H]WIN 35,428 binding was specific, saturable, and to a single class of binding sites with an estd.  $K_m/V_{max}$  of .apprx.2 . $\mu$ M and 6 pmol/min/105 cells for DA uptake and  $K_d/B_{max}$  values of .apprx.10 nM and 113 fmol/105 cells for [3H]WIN 35,428. [3H]DA uptake was inhibited in a concn.-dependent and uniphasic manner by dopaminergic agents with an appropriate rank order of potency for the DA transporter. Although most uptake blockers inhibited [3H]WIN 35,428 binding in a uniphasic manner, WIN 35,428, Lu 19,005, D-amphetamine, and DA clearly displayed the presence of both high and low affinity components. Comparison of the  $K_i$  values for the inhibition of [3H]DA uptake with [3H]WIN 35,428 binding reveals that, for uptake blockers and D-amphetamine, it is the high affinity component that shares pharmacol. identity with effects on DA uptake ( $r = 0.9985$ ), whereas for DA it is the low affinity site. In striking contrast, however, [3H]GBR 12,935 binding to COS-7 cells could not be made to exhibit a pharmacol. profile indicative of the DA transporter and suggests that the site regulating functional [3H]DA uptake may not be identical with sites labeled by [3H]GBR 12,935 in these cells. Moreover, these sites appear unrelated to those previously described in native membranes as "piperazine acceptor" or P 450 proteins. Comparison of  $K_i$  values and rank order of potency for the inhibition of [3H]WIN 35,428 or [3H]GBR 12,935 binding to human caudate membranes reveals pharmacol. homol., but not identity, with that of the cloned DA uptake process. Taken together, these data suggest that 1) [3H]WIN 35,428 recognizes two sites of the DA transporter, of which only one appears to represent the functional state of the protein, and 2) [3H]WIN 35,428 and [3H]GBR 12,935 do not appear to bind the same functional form/state of the DA transporter. Whether the nonidentity of binding sites is a manifestation of some post-translational regulatory event (e.g., phosphorylation/accessory binding protein) or caused by the existence of multiple mol. forms of the DA transporter is currently unknown.  
IT 50560-38-8 50560-45-7  
RL: BIOL (Biological study)  
(dopamine transporter of humans function and GBR 12,935 and WIN 35,428 binding response to)  
RN 50560-38-8 CAPLUS  
CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-, (4S)- (9CI) (CA INDEX NAME)

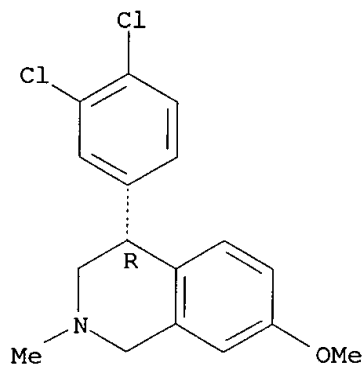
Absolute stereochemistry.



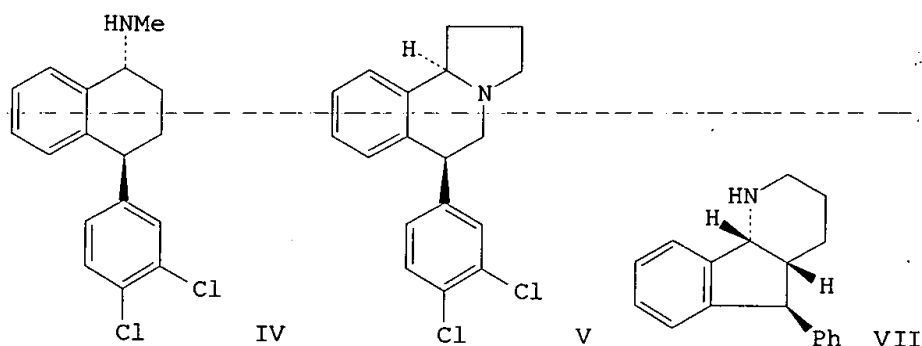
RN 50560-45-7 CAPLUS

CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-  
, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L48 ANSWER 23 OF 100 CAPLUS COPYRIGHT 2003 ACS  
 AN 1993:616751 CAPLUS  
 DN 119:216751  
 TI Conformational analysis of cocaine, the potent analog 2.beta.-carbomethoxy-3.beta.-(4-fluorophenyl)tropane (CFT), and other dopamine reuptake blockers  
 AU Froimowitz, Mark  
 CS McLean Hosp., Harvard Med. Sch., Belmont, MA, 02178, USA  
 SO Journal of Computational Chemistry (1993), 14(8), 934-43  
 CODEN: JCCHDD; ISSN: 0192-8651  
 DT Journal  
 LA English  
 GI

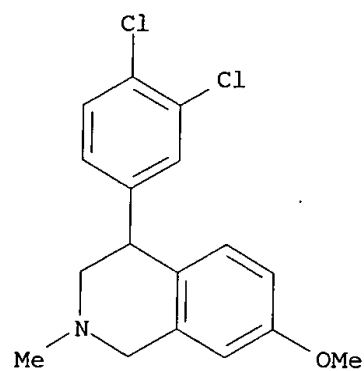


AB By using the MM2-87 program and parameter set, conformational analyses were performed on cocaine (I), the potent analog 2.beta.-carbomethoxy-3.beta.-(4-fluorophenyl)tropane (CFT, II), and a group of dopamine reuptake blockers that contain 2 Ph rings. The latter includes LU 19-005 (III), a 1-amino-4-phenyltetralin (IV), a hexahydropyrrolo[2,1-b]isoquinoline (V), diclofensine (VI), and a hexahydro[1,2-b]pyridine (VII). As detd. by using different values for the dielec. const., the global min. of I and II is a conformer in which there is a favorable electrostatic interaction between the ammonium hydrogen and the carbonyl of the carbomethoxy group. The N-Me groups in I and II strongly prefer the equatorial position of the piperidine ring. These results were also related to 4 crystal structures of I and its close derivs. III-VII have a common conformation that was used to define the pharmacophore for dopamine reuptake blockers including the required orientation of the ammonium hydrogen. The pharmacophore provides an explanation of why the tertiary amine analogs of III and IV are less potent than the secondary amines because the added N-Me group occupies the position required for the ammonium hydrogen. This explanation, however, does not work for VII, in which the tertiary amine is again less active than the secondary amine. However, this last series appears to have a no. of anomalous features. Superposition of II with the pharmacophore suggests that its carbomethoxy group may occupy the same region of the receptor as the 2nd Ph ring in III-VII.

IT **67165-56-4**, Diclofensine  
 RL: PROC (Process)  
 (conformational anal. of)  
 RN 67165-56-4 CAPLUS  
 CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-

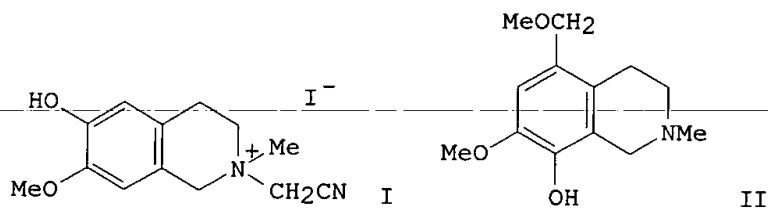
09/704,306

(9CI) (CA INDEX NAME)



09/704,306

~~L48~~ ANSWER 24 OF 100 CAPLUS COPYRIGHT 2003 ACS  
~~MN~~ 1993:255160 CAPLUS  
DN 118:255160  
TI A novel rearrangement of N-cyanomethylhydroxytetrahydroisoquinolinium  
methiodides under basic conditions  
AU Hara, Hiroshi; Endoh, Masaki; Kaneko, Kenichi; Hoshino, Osamu  
CS Fac. Pharm. Sci., Sci. Univ. Tokyo, Tokyo, 162, Japan  
SO Heterocycles (1993), 36(2), 249-52  
CODEN: HTCYAM; ISSN: 0385-5414  
DT Journal  
LA English  
OS CASREACT 118:255160  
GI

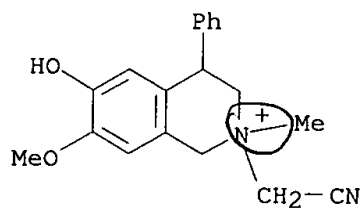


AB Reaction of N-(cyanomethyl)isoquinolinium methiodide (I) with sodium methoxide gave a rearranged tetrahydroisoquinolin-8-ol (II) in high yield. With 1- or 4-substituted N-cyanomethylisoquinolinium and 8-hydroxytetrahydroisoquinolinium methiodides, similar rearrangement was obsd. Plausible mechanism on formation of the products was discussed.

IT **147734-10-9P 147734-14-3P**  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and rearrangement of)

RN 147734-10-9 CAPLUS

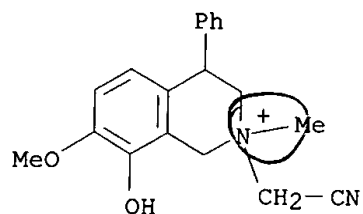
CN Isoquinolinium, 2-(cyanomethyl)-1,2,3,4-tetrahydro-6-hydroxy-7-methoxy-2-methyl-4-phenyl-, iodide (9CI) (CA INDEX NAME)



RN 147734-14-3 CAPLUS

CN Isoquinolinium, 2-(cyanomethyl)-1,2,3,4-tetrahydro-8-hydroxy-7-methoxy-2-methyl-4-phenyl-, iodide (9CI) (CA INDEX NAME)



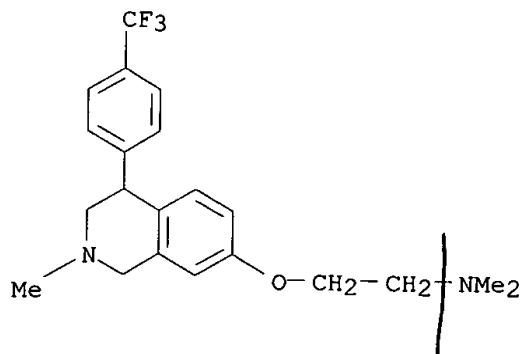


● I<sup>-</sup>

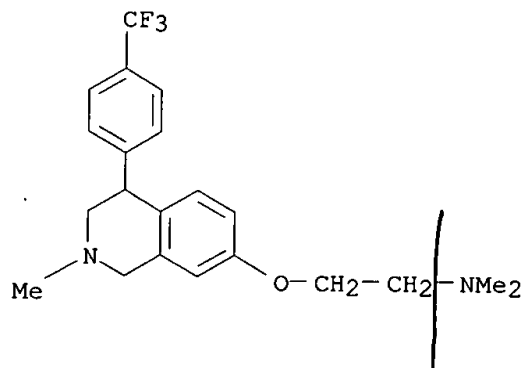
IT 147750-34-3P 147750-38-7P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 RN 147750-34-3 CAPLUS  
 RN 147750-38-7 CAPLUS  
 -----IT 88741-58-6-----  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reaction of, with iodoacetonitrile)  
 RN 88741-58-6 CAPLUS

09/704,306

~~L48~~ ANSWER 25 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1993:204694 CAPLUS  
DN 118:204694  
TI Multivariate quantitative structure-toxicity relationships in a series of dopamine mimetics  
AU Ridings, James E.; Manallack, David T.; Saunders, Martin R.; Baldwin, John A.; Livingstone, David J.  
CS SmithKline Beecham Pharm., Frythe/Welwyn/Herts., AL6 9AR, UK  
SO Toxicology (1992), 76(3), 209-17  
CODEN: TXCYAC; ISSN: 0300-483X  
DT Journal  
LA English  
AB The techniques of principal components anal. and non-linear mapping are routinely used by computer chemists at SmithKline Beecham Pharmaceuticals in the process of drug development by relating the structure of a compd. to its chem. activity. These techniques had not previously been applied to the assocn. between the structure of a compd. and its toxicol. properties. Using a series of 12 structurally related compds. (11 were active dopamine mimetics and one was inactive), of which five were known to be teratogenic and seven were non-teratogenic, it was possible to demonstrate that mol. modeling techniques could be applied to differentiate toxicol. data. The structure/property relationships of these compds. were investigated using calcd. physicochem. properties, mol. modeling and multivariate statistical techniques. A data set of 56 mol. descriptors was used to represent this series of compds. Anal. of the data set using principal components anal. and non-linear mapping suggested that teratogenicity was assocd. with four mol. properties. Moreover, the electronic nature of the 4-Ph group appeared to be an important determinant of the teratogenesis.  
IT **62888-75-9**  
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (teratogenicity of, structure in relation to)  
RN 62888-75-9 CAPLUS  
CN Ethanamine, N,N-dimethyl-2-[[1,2,3,4-tetrahydro-2-methyl-4-[4-(trifluoromethyl)phenyl]-7-isoquinolinyloxy]- (9CI) (CA INDEX NAME)



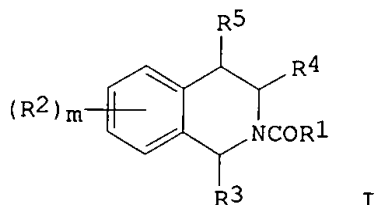
148 ANSWER 26 OF 100 CAPLUS COPYRIGHT 2003 ACS  
 AN 1993:204693 CAPLUS  
 DN 118:204693  
 TI A qualitative assessment of developmental toxicity within a series of structurally related dopamine mimetics  
 AU Ridings, James E.; Baldwin, John A.  
 CS SmithKline Beecham Pharm., Frythe/Welwyn/Herts., AL6 9AR, UK  
 SO Toxicology (1992), 76(3), 197-207  
 CODEN: TXCYAC; ISSN: 0300-483X  
 DT Journal  
 LA English  
 AB A qual. assessment of developmental toxicity within a series of 12 structurally related compds., 11 of which were active dopamine mimetics and one was inactive, was conducted in rats treated orally by gavage during the major period of organogenesis. Doses were chosen where possible to be equipotent in terms of pharmacol. activity. The series was typified by the compd. BRL 16644 (2-[[3,4-dihydro-2,2-dimethyl-4-[3-(trifluoromethyl)phenyl]-2H-1-benzopyran-7-yl]oxy]-N,N-dimethylethanamine). Five of these compds. were clearly teratogenic producing specific abnormalities typified by anasarca, brachygnathia and cleft palate. Similar levels of maternal toxicity, particularly stereotypic behavior, and fetotoxicity were seen in both teratogenic and nonteratogenic compds. suggesting that neither maternal nor fetotoxicity plays a role in the etiol. of the abnormalities. Four of the teratogenic compds. contained a trifluoromethyl group in the 4-Ph ring and, within this series of compds., substitution with this group appears to confer teratogenicity. Although equipotent doses were used this only pertained to the adult and as only limited pharmacokinetic data were available, including the extent of placental transfer, the influence of this group is not clear. Investigations have been undertaken to relate the teratogenic potential of these compds. to a no. of their chem. descriptors, including electronic, steric, quantum chem. and hydrophobicity parameters, to try and clarify the influence of the trifluoromethyl group.  
 IT 62888-75-9  
 RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (teratogenicity of, structure in relation to)  
 RN 62888-75-9 CAPLUS  
 CN Ethanamine, N,N-dimethyl-2-[[1,2,3,4-tetrahydro-2-methyl-4-[4-(trifluoromethyl)phenyl]-7-isoquinolinyl]oxy]- (9CI) (CA INDEX NAME)



09/704,306

~~DB~~ ANSWER 27 OF 100 CAPLUS COPYRIGHT 2003 ACS  
~~IN~~ 1992:550904 CAPLUS  
~~DN~~ 117:150904  
TI Preparation of N-acyltetrahydroisoquinolines as inhibitors of  
acyl-coenzyme A: cholesterol acyltransferase  
IN Dugar, Sundee; Kogan, Timothy  
PA Schering Corp., USA  
SO U.S., 9 pp.  
CODEN: USXXAM  
DT **Patent**  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5124337	A	19920623	US 1991-702993	19910520
	US 5238935	A	19930824	US 1992-839522	19920220
	EP 514851	A1	19921125	EP 1992-108460	19920519
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, PT, SE				
	JP 07002785	A2	19950106	JP 1992-127144	19920520
	JP 07030028	B4	19950405		
PRAI	US 1991-702993		19910520		
OS	MARPAT 117:150904				
GI					



AB The compds. I [R1 = C10-25 alkyl which may be substituted and/or may be interrupted by O, SOp, NH, CO, etc.; R1 may also contain double bonds; p = 0-2; R1 does not contain an amide linkage; each R2 = OH, C1-6 alkyl, C1-6 alkoxy, halo, amino, (di)C1-6 alkylamino; R3-R5 = H, (CH2)nAr; Ar = (substituted) Ph, -heteroaryl; n = 0-2; m = 0-2] were prepd. as acyl CoA-cholesterol acyltransferase (II) inhibitors useful as antiatherosclerotics. Thus, ring-opening of styrene oxide by 3,4-dimethoxybenzylamine followed by cyclization of the resultant hydroxyamine in the presence of MeSO3H gave 6,7-dimethoxy-4-phenyl-1,2,3,4-tetrahydroisoquinoline as the mesylate salt. To a soln. of the latter in Et2O contg. Et3N was added oleoyl chloride at 0.degree. and the mixt. was stirred 2-5 h at 0.degree. to give title compd. I [R1 = (Z)-(CH2)7CH:CH(CH2)7Me; R2 = OMe at 6- and 7-position of isoquinoline ring; R3,R4 = H; R5 = Ph; m = 2] (III). The IC50 of III against II was 2.4 .mu.M. Formulations contg. I were prepd.

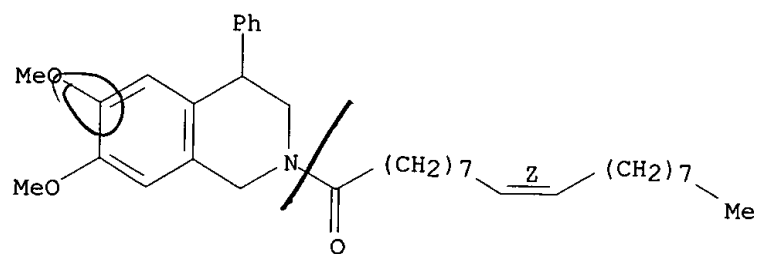
IT **143102-62-9P**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of, as cholesterol acyltransferase inhibitor)

RN 143102-62-9 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-6,7-dimethoxy-2-(1-oxo-9-octadecenyl)-4-phenyl-, (Z)- (9CI) (CA INDEX NAME)

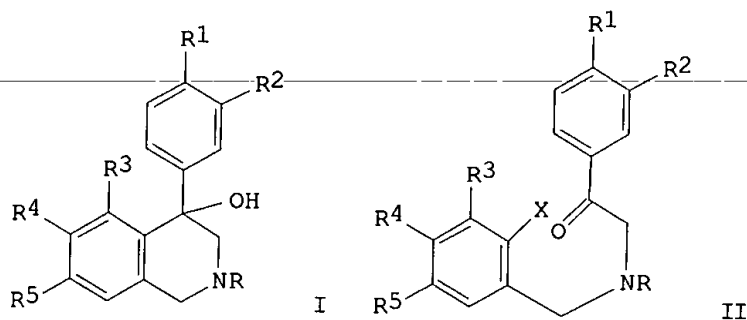
09/704,306

Double bond geometry as shown.

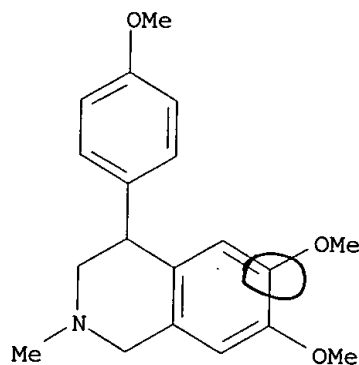


09/704,306

~~148~~ ANSWER 28 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1992:214309 CAPLUS  
DN 116:214309  
TI A convenient synthesis of 4-substituted 1,2,3,4-tetrahydroisoquinolin-4-ols by a novel intramolecular Barbier reaction and by an insertion reaction: reaction scope and limitations  
AU Kihara, Masaru; Kashimoto, Minoru; Kobayashi, Yoshimaro  
CS Fac. Pharm. Sci., Univ. Tokushima, Tokushima, 770, Japan  
SO Tetrahedron (1992), 48(1), 67-78  
CODEN: TETRAB; ISSN: 0040-4020  
DT Journal  
LA English  
OS CASREACT 116:214309  
GI



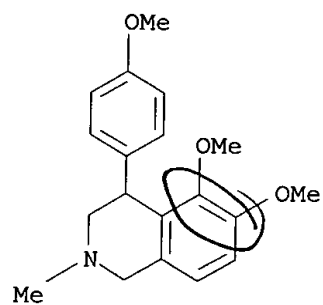
AB 4-Substituted 1,2,3,4-tetrahydroisoquinolin-4-ols (I) were prepd. from N-(2-iodobenzyl)phenacylamines II (X = I, Br) by an intramol. Barbier reaction with BuLi and by an insertion reaction with zerovalent Ni. Approx. 20 I (R = Me, Et, Bu, CH<sub>2</sub>Ph; R<sub>1</sub> = H, Br, F, Cl, Et, OMe; R<sub>2</sub> = H, Cl, CF<sub>3</sub>; R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub> = H, OMe) were prepd.  
IT **66395-91-3P 115888-85-2P**  
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (prepn. and spectra of)  
RN 66395-91-3 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-6,7-dimethoxy-4-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



09/704,306

RN 115888-85-2 CAPLUS

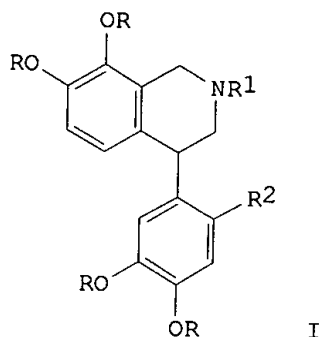
CN Isoquinoline, 1,2,3,4-tetrahydro-5,6-dimethoxy-4-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



09/704,306

~~1~~8 ANSWER 29 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1992:188092 CAPLUS  
DN 116:188092  
TI Preparation of tetrahydroisoquinoline derivatives as active oxygen scavengers  
IN Tanaka, Akihiro; Yokota, Masaki; Yazawa, Shusuke; Asano, Masaharu  
PA Yamanouchi Pharmaceutical Co., Ltd., Japan  
SO Jpn. Kokai Tokkyo Koho, 12 pp.  
CODEN: JKXXAF  
DT Patent  
LA Japanese  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 03294268	A2	19911225	JP 1990-95958	19900410
PRAI	JP 1990-95958		19900410		
OS	MARPAT 116:188092				
GI					



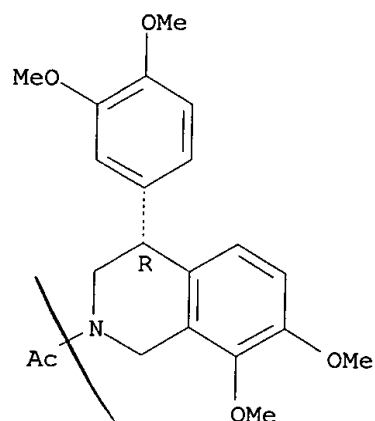
AB The title derivs. I (R = H; R1 = H, lower alkyl, acyl, alkenyl; R2 = H, halo, lower alkyl) or their salts are active O scavengers. I are useful for treatment of inflammatory diseases, burn, arthritis, rheumatism, pancreatitis, cataract, anticancer agents-assocd. side effects, acute cardiac infarction, radiation damage, etc. A MeOH soln. of 0.91 g 2,4,5-Cl(MeO)2C6H2CH(OH)CH2NH2 and 0.72 g 2,3-(MeO)2C6H3CHO was refluxed for 30 min then treated with NaBH4 to give 1.44 g 2,4,5-Cl(MeO)2C6H2CH(OH)CH2NHCH2C6H3(OMe)2-2,3. The product (1.4 g) in CF3CO2H was treated with H2SO4 at 0.degree. for 40 min to give 1.21 g II (I: R = Me, R1 = H, R2 = Cl), 0.65 g of which in CH2Cl2 was treated with BBr3 stirred at room temp. for 3 h to give 0.57 g III. III.HBr showed scavenging activity with IC50 value 1.5.times.10-6 M. A tablet contg. III 50, cryst. cellulose 75, lactose 60, partial .alpha.-starch 12, talc 2, and Mg stearate 1 mg was prepd.

IT 138085-95-7P 138085-96-8P 140406-48-0P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and deprotection of)  
RN 138085-95-7 CAPLUS  
CN Isoquinoline, 2-acetyl-4-(3,4-dimethoxyphenyl)-1,2,3,4-tetrahydro-7,8-dimethoxy-, (R)- (9CI) (CA INDEX NAME)



09/704,306

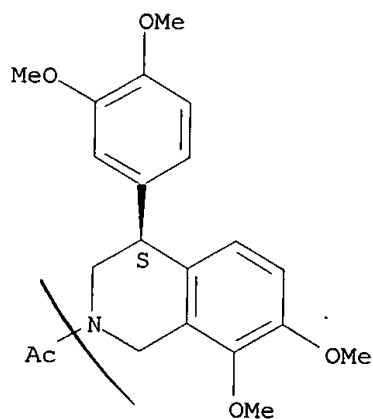
Absolute stereochemistry.



~~RN 138085-96-8 CAPLUS~~

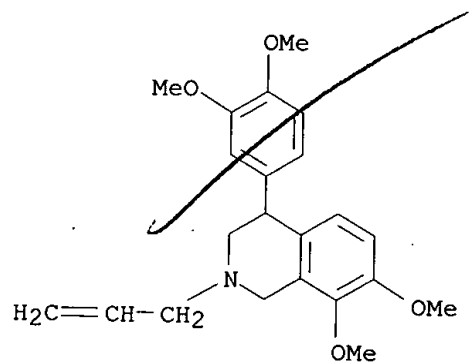
CN Isoquinoline, 2-acetyl-4-(3,4-dimethoxyphenyl)-1,2,3,4-tetrahydro-7,8-dimethoxy-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 140406-48-0 CAPLUS

CN Isoquinoline, 4-(3,4-dimethoxyphenyl)-1,2,3,4-tetrahydro-7,8-dimethoxy-2-(2-propenyl)-, hydrobromide (9CI) (CA INDEX NAME)



● HBr

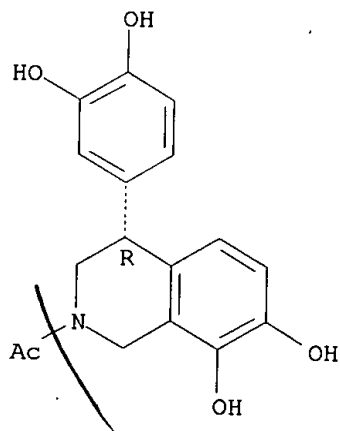
IT 138085-97-9P 138085-98-0P 140406-52-6P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of, as active oxygen scavenger)

RN 138085-97-9 CAPLUS

CN 7,8-Isoquinolinediol, 2-acetyl-4-(3,4-dihydroxyphenyl)-1,2,3,4-tetrahydro-, (R)- (9CI) (CA INDEX NAME)

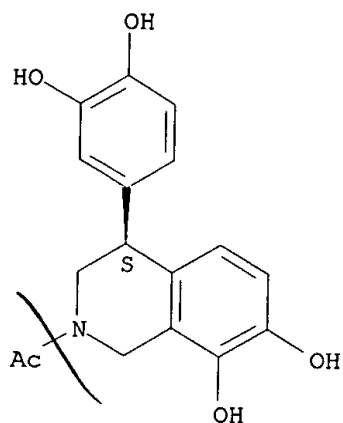
Absolute stereochemistry.



RN 138085-98-0 CAPLUS

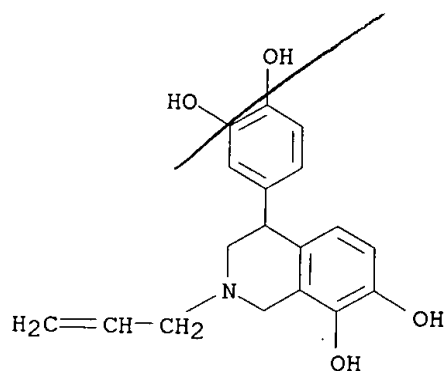
CN 7,8-Isoquinolinediol, 2-acetyl-4-(3,4-dihydroxyphenyl)-1,2,3,4-tetrahydro-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 140406-52-6 CAPLUS

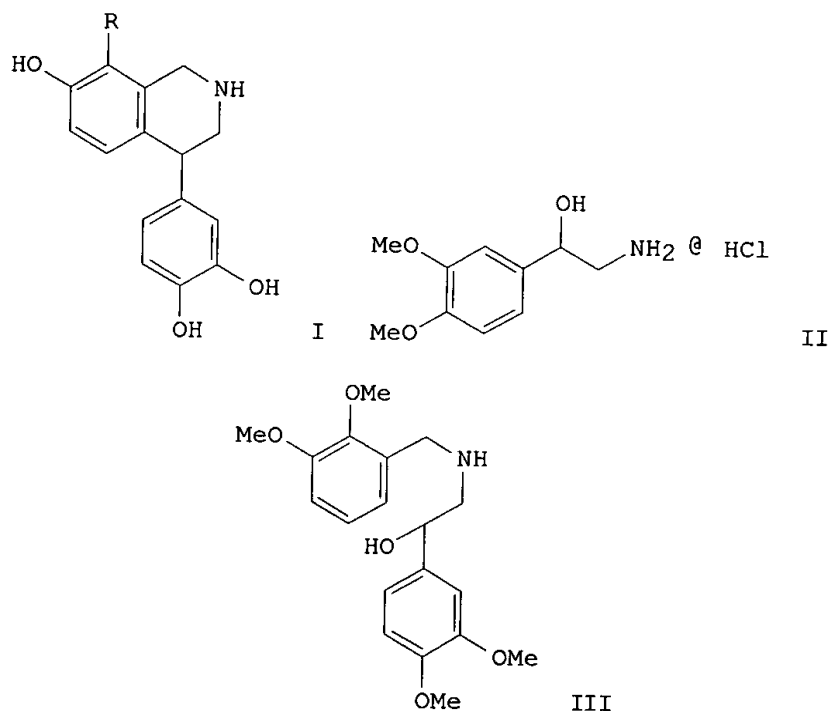
CN 7,8-Isoquinolinediol, 4-(3,4-dihydroxyphenyl)-1,2,3,4-tetrahydro-2-(2-propenyl)-, hydrobromide (9CI) (CA INDEX NAME)



● HBr

09/704,306

L48 ANSWER 30 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1992:128616 CAPLUS  
DN 116:128616  
TI Synthesis, resolution, and renal vasodilation activity of novel DA1  
agonists: 4-(3,4-dihydroxyphenyl)-1,2,3,4-tetrahydroisoquinoline  
derivatives  
AU Anan, Hideki; Tanaka, Akihiro; Tsuzuki, Ryuji; Yokota, Masaki; Yatsu,  
Takeyuki; Honda, Kazuo; Asano, Masaharu; Fujita, Shigeo; Furuya, Toshio;  
Fujikura, Takashi  
CS Cent. Res. Lab., Yamanouchi Pharm. Co., Ltd., Tsukuba, 305, Japan  
SO Chemical & Pharmaceutical Bulletin (1991), 39(11), 2910-14  
CODEN: CPBTAL; ISSN: 0009-2363  
DT Journal  
LA English  
OS CASREACT 116:128616  
GI



AB Title compds. I (R = OH, Me) were prepd. in the racemic form and the optically active forms (S)-(-)- and (R)-(+)-I (R = OH), (S)-(+)- and (R)-(-)-I (R = Me). Thus, condensation of 2,3-dimethoxybenzaldehyde with (methoxyphenyl)aminoethanol II gave [[(dimethoxybenzyl)amino]methyl]benzyl alc. III which cyclized and was treated with 48% HBr to give (+)-I (R = OH). They were tested for renal vasodilation activity.

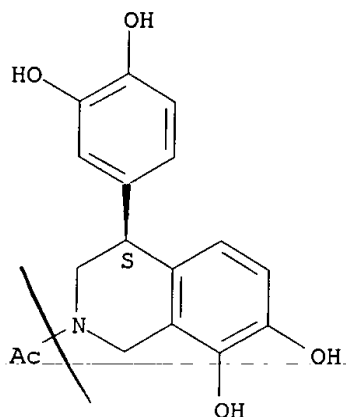
IT **138085-98-OP**  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and deacetylation of)

09/704,306

RN 138085-98-0 CAPLUS

CN 7,8-Isoquinolinediol, 2-acetyl-4-(3,4-dihydroxyphenyl)-1,2,3,4-tetrahydro-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



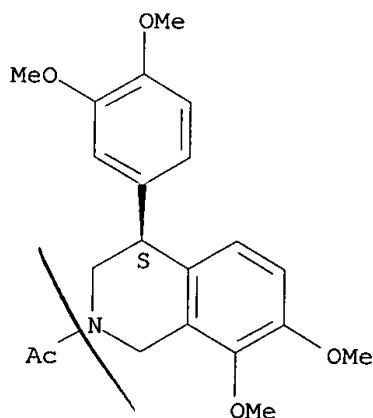
IT 138085-96-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (prepn. and demethylation of)

RN 138085-96-8 CAPLUS

CN Isoquinoline, 2-acetyl-4-(3,4-dimethoxyphenyl)-1,2,3,4-tetrahydro-7,8-dimethoxy-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



09/704,306

~~DA~~ 8 ANSWER 31 OF 100 CAPLUS COPYRIGHT 2003 ACS

~~AN~~ 1992:59235 CAPLUS

DN 116:59235

TI Preparation of tetrahydroisoquinoline derivatives as oxygen scavengers

IN Asano, Masaharu; Yazawa, Shusuke; Tanitsu, Takeyuki; Arai, Yukinori;  
Tanaka, Akihiro

PA Yamanouchi Pharmaceutical Co., Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 23 pp.

CODEN: JKXXAF

DT **Patent**

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 03190818	A2	19910820	JP 1989-332126	19891221
	JP 2851332	B2	19990127		
PRAI	JP 1989-332126		19891221		

OS MARPAT 116:59235

GI For diagram(s), see printed CA Issue.

AB The title compds. [I; ring A = Q (wherein R1 = H, alkyl, OH, halo, amino, acylamino; R2 = OH, alkylsulfonylamino, amino), Q1, Q2 (wherein R3, H, alkylsulfonyl); R = H, halo], effective O scavengers useful as antiinflammatory agents, are prepd. Refluxing a mixt. of 1.0 g II, 0.85 g 2,3-(MeO)2C6H3CHO, and 0.63 mL Et3N in MeOH gave 1.07 g III, which (1.0 g) was dissolved in CF3CO2H and treated with concd. H2SO4 under cooling to give 560 mg IV after hydrolysis with 48% HBr. IV showed much superior antioxidant activity, as super oxide anion radical scavenger, than catechol. Capsule and tablet formulations were given.

IT 119085-55-1P 138085-95-7P 138085-96-8P

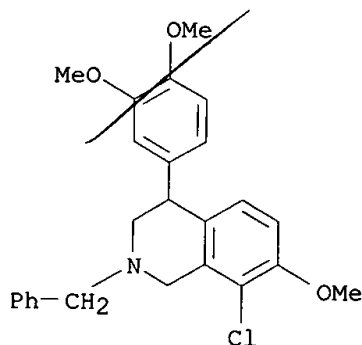
138085-97-9P 138085-98-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and reaction of, in prepn. of oxygen scavenger)

RN 119085-55-1 CAPLUS

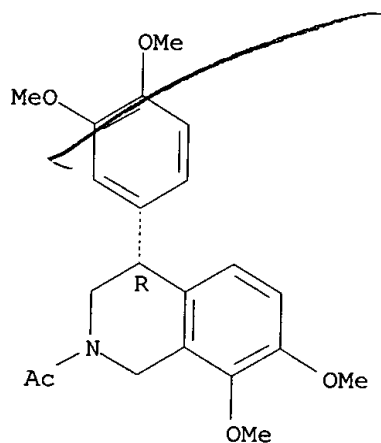
CN Isoquinoline, 8-chloro-4-(3,4-dimethoxyphenyl)-1,2,3,4-tetrahydro-7-methoxy-2-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 138085-95-7 CAPLUS

CN Isoquinoline, 2-acetyl-4-(3,4-dimethoxyphenyl)-1,2,3,4-tetrahydro-7,8-dimethoxy-, (R)- (9CI) (CA INDEX NAME)

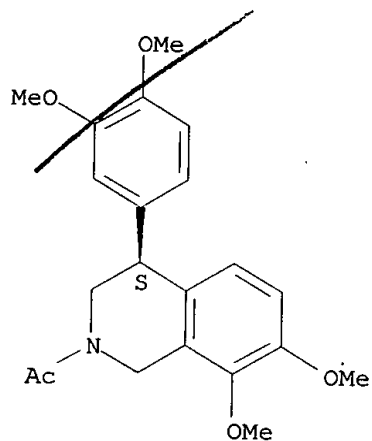
Absolute stereochemistry.



RN 138085-96-8 CAPLUS

CN Isoquinoline, 2-acetyl-4-(3,4-dimethoxyphenyl)-1,2,3,4-tetrahydro-7,8-dimethoxy-, (S)- (9CI) (CA INDEX NAME)

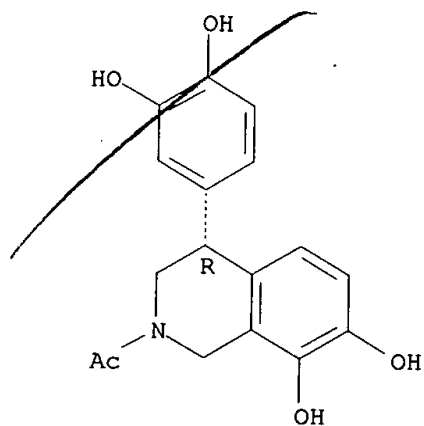
Absolute stereochemistry.



RN 138085-97-9 CAPLUS

CN 7,8-Isoquinolinediol, 2-acetyl-4-(3,4-dihydroxyphenyl)-1,2,3,4-tetrahydro-, (R)- (9CI) (CA INDEX NAME)

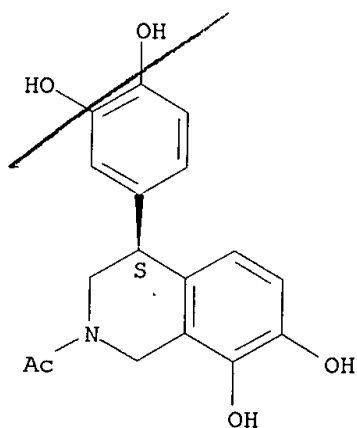
Absolute stereochemistry.



RN 138085-98-0 CAPLUS

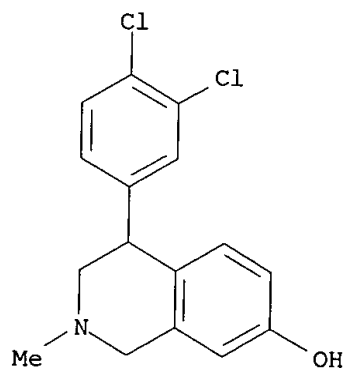
CN 7,8-Isoquinolinediol, 2-acetyl-4-(3,4-dihydroxyphenyl)-1,2,3,4-tetrahydro-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.





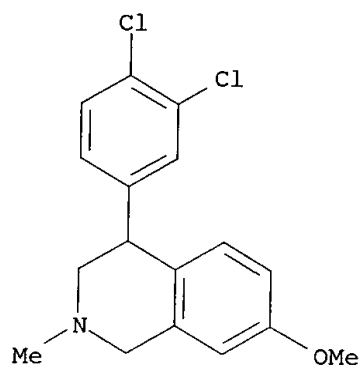
L48 ANSWER 32 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1992:19436 CAPLUS  
DN 116:19436  
TI Antigenic determinants responsible for the reactions of drug-dependent antibodies with blood cells  
AU Salama, A.; Santoso, S.; Mueller-Eckhardt, C.  
CS Inst. Clin. Immunol., Justus Liebig Univ., Giessen, D-6300, Germany  
SO British Journal of Haematology (1991), 78(4), 535-9  
CODEN: BJHEAL; ISSN: 0007-1048  
DT Journal  
LA English  
AB To det. the antigenic combining sites of drug-dependent antibodies in patients with drug-related immunohemolysis, the reactivity of 35 nomifensine-induced antibodies was assessed against human red blood cells (RBC) in the presence of 11 closely related compds.: nomifensine (I), its 3 main metabolites including their methoxylated analogs, and diclofensine with its 3 main metabolites. Three types of antibody reactivity patterns could be differentiated: (1) antibodies most strongly reactive with I (n = 12); (2) antibodies primarily directed against one of its main metabolites (n = 7); (3) antibodies optimally reactive with its unknown metabolites (n = 16). The antibodies preferentially directed against I showed varying cross-reactions with I-related compds. and in almost all cases also with diclofensine and/or its metabolites. Those antibodies which were optimally reactive with metabolites reacted only with I-derived compds. and only 1 of them was noncrossreactive. The 3rd group of antibodies showed no (n = 12) or only weak (n = 4) cross reactions with I and/or its metabolites. RBC antigens were required for the reaction in .apprx.40% of all antibodies, independent of their reactivity with the compds. Thus, even when the specificity of some antibodies appeared to be predominantly controlled by certain structural features of the compds., the actual antigenic combining site of each antibody was different and seemed to comprise parts of the drug-related determinants as well as different constituents on RBC membranes. RBCs function as carrier-like macromols., since they are directly involved in the reaction. The drugs and their metabolites act as pseudohaptens, inasmuch as they do not bind tightly to the cells. The determinants which govern the immune response result from an accidental attachment rather than from a predetd. selection of antigenic membrane structures, since each antibody shows a unique reaction pattern.  
IT 34041-52-6 67165-56-4, Diclofensine  
RL: PRP (Properties)  
(antibody combining sites for erythrocyte antigens in nomifensine-related immune hemolysis cross-reaction with)  
RN 34041-52-6 CAPLUS  
CN 7-Isoquinolinol, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-2-methyl- (8CI, 9CI) (CA INDEX NAME)



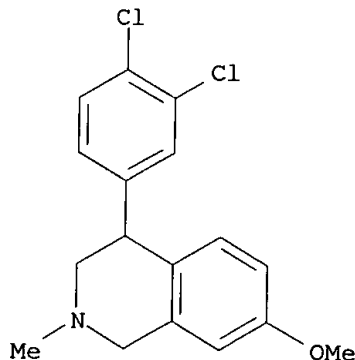
RN 67165-56-4 CAPLUS

CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-  
(9CI) (CA INDEX NAME)

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L48 ANSWER 33 OF 100 CAPLUS COPYRIGHT 2003 ACS  
 AN 1991:663334 CAPLUS  
 DN 115:263334  
 TI Mixed micelles as a proliposomal, lymphotropic drug carrier  
 AU Supersaxo, Andreas; Hein, Wayne R.; Steffen, Hans  
 CS F. Hoffmann-La Roche Ltd., Basel, CH-4002, Switz.  
 SO Pharmaceutical Research (1991), 8(10), 1286-91  
 CODEN: PHREEB; ISSN: 0724-8741  
 DT Journal  
 LA English  
 AB Four lipophilic, low-mol.-wt. drugs solubilized in phosphatidylcholine-bile salt mixed micelles were injected s.c. into the hind legs of sheep and their cumulative recoveries in lymph draining from the site of application were detd. Surprisingly, the cumulative recoveries (percentage of dose) varied between <1 and 60%. There is a correlation between the lipophilicity of the drug (log P octanol/water - Rm.degree. value) and the proportion of the dose adsorbed by the lymphatic route. Drugs with Rm.degree. values >10 are absorbed preferentially by the lymphatics (>50% of dose), whereas compds. with Rm.degree. values <4 are hardly absorbed at all by the lymphatics (<10% of dose). By applying the prodrug principle it was demonstrated that it is also possible to target drugs with Rm.degree. values <4 to the lymphatics. Furthermore, the anal. of the collected lymph samples by gel filtration, quasi-elastic light scattering, and electron microscopy revealed that, following s.c. administration, mixed micelles are converted into homogeneous, unilamellar vesicles. Mixed micelles may represent a suitable delivery system for low-mol.-wt. drugs whose targets are lymphoid cells. In addnl, for drugs where liposomal application leads to a therapeutic advantage, the thermodynamically stable mixed micelle could be a good alternative to be liposome. However, for both applications a high drug-lipophilicity is a prerequisite.  
 IT **67165-56-4, Diclofensine**  
 RL: BIOL (Biological study)  
 (mixed micelles as proliposomal lymphotropic carrier of, for s.c. administration)  
 RN 67165-56-4 CAPLUS  
 CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl- (9CI) (CA INDEX NAME)



L48 ANSWER 34 OF 100 CAPLUS COPYRIGHT 2003 ACS

AN 1991:575763 CAPLUS

DN 115:175763

TI Effects of reuptake inhibitors on dopamine release from the stalk-median eminence and posterior pituitary in vitro

AU Garris, Paul A.; Ben-Jonathan, Nira

CS Sch. Med., Indiana Univ., Indianapolis, IN, 46223, USA

SO Brain Research (1991), 556(1), 123-9

CODEN: BRREAP; ISSN: 0006-8993

DT Journal

LA English

AB Similar to other dopaminergic systems, the dopaminergic neurons innervating the stalk-median eminence (SME) and posterior pituitary (PP) possess an uptake mechanism for dopamine (DA). However, the extent of DA reuptake in these tissues and its physiol. significance are debated since much of the released DA is removed by the hypophyseal portal vasculature before recapture. The objectives of this study were: (1) to establish in vitro conditions for examg. the effects of reuptake inhibitors on DA release from the PP and SME; (2) to compare the effects of nomifensine, diclofensine, and amphetamine on DA release from the SME and PP; and (3) to distinguish between reuptake and releasing properties of these drugs. Individual SME and PP were dissected from ovariectomized rats and incubated in either a static or perfusion system. Media DA was extd. with alumina and quantitated by high-performance liq. chromatog. with electrochem. detection. The reuptake inhibitors nomifensine, diclofensine, and amphetamine, in the presence of the monoamine oxidase inhibitor pargyline, stimulated both basal and K+-evoked release of DA from the SME and PP under static incubation conditions. The drugs elicited a 2-3-fold higher increase in basal DA release from the SME than from the PP. Amphetamine stimulated DA release in the perfusion system, whereas nomifensine and diclofensine were without effects. Thus, a mechanism for the reuptake of DA is operable in both the SME and PP, and the reuptake of DA appears to be more active in the SME than the PP. Unlike amphetamine, nomifensine and diclofensine are pure reuptake inhibitors devoid of direct DA-releasing activities.

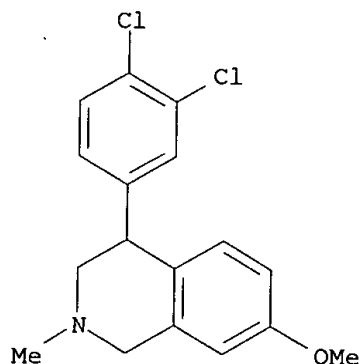
IT 67165-56-4, Diclofensine

RL: BIOL (Biological study)

(dopamine release and reuptake response to, in brain and posterior pituitary)

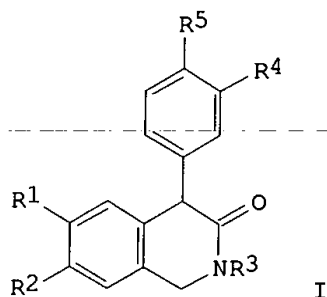
RN 67165-56-4 CAPLUS

CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-(9CI) (CA INDEX NAME)



09/704,306

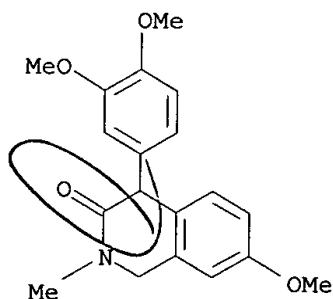
18 ANSWER 35 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1991:471363 CAPLUS  
DN 115:71363  
TI Synthesis of 4-aryl-1,4-dihydro-3(2H)-isoquinolinones by oxidative  
cyclization of N-benzylarylacetamides  
AU Venkov, A.; Vodenicharov, D.; Ivanov, I.  
CS Dep. Chem., Univ. Plovdiv, Plovdiv, 4000, Bulg.  
SO Synthesis (1991), (6), 476-8  
CODEN: SYNTBF; ISSN: 0039-7881  
DT Journal  
LA English  
GI



AB Seven title compds. I [R1, R2, R4, R5 = H, MeO; R3 = Me, Et, PhCH2, 3,4-(MeO)2C6H3CH2CH2] were prepd. via oxidative cyclization of 3,4-R4R5C6H3CH2CONR3CH2C6H3R1R2-4,3 (II) by Pb(OAc)4 in AcOH-F3CCO2H. II were prepd. in one-pot by the condensation of 4,3-R1R2C6H3CHO and R3NH2 followed by redn. with NaBH4 and subsequent acylation with 3,4-R4R5C6H3CH2COCl. Thus, I (R1 = R2 = H, R3 = Me, R4 = R5 = OMe) was prepd. in 85% yield from II.

IT **135182-07-9P 135182-08-0P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

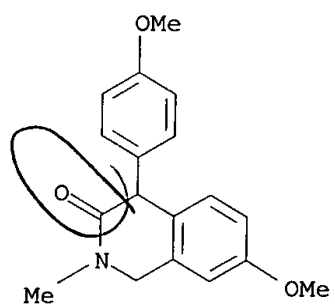
RN 135182-07-9 CAPLUS  
CN 3(2H)-Isoquinolinone, 4-(3,4-dimethoxyphenyl)-1,4-dihydro-7-methoxy-2-methyl- (9CI) (CA INDEX NAME)



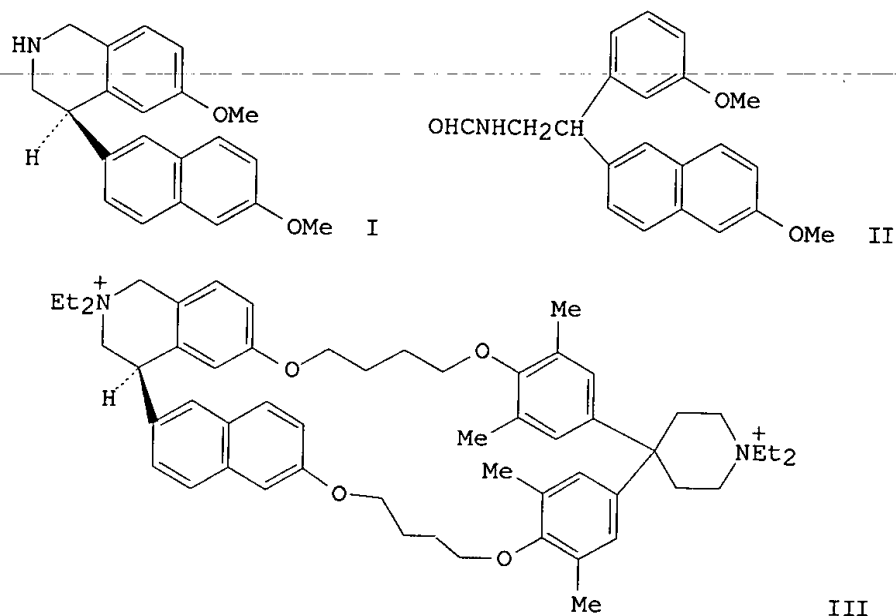
RN 135182-08-0 CAPLUS  
CN 3(2H)-Isoquinolinone, 1,4-dihydro-7-methoxy-4-(4-methoxyphenyl)-2-methyl-

09/704,306

(9CI) (CA INDEX NAME)



118 ANSWER 36 OF 100 CAPLUS COPYRIGHT 2003 ACS  
 AN 1991:229195 CAPLUS  
 DN 114:229195  
 TI Synthesis and complexation properties of a water-soluble optically active cyclophane incorporating a 4-naphthyl-1,2,3,4-tetrahydroisoquinoline unit as a chiral spacer  
 AU Georgiadis, Taxiarchis M.; Georgiadis, Millie M.; Diederich, Francois  
 CS Dep. Chem. Biochem., Univ. California, Los Angeles, CA, 90024-1569, USA  
 SO Journal of Organic Chemistry (1991), 56(10), 3362-9  
 CODEN: JOCEAH; ISSN: 0022-3263  
 DT Journal  
 LA English  
 OS CASREACT 114:229195  
 GI



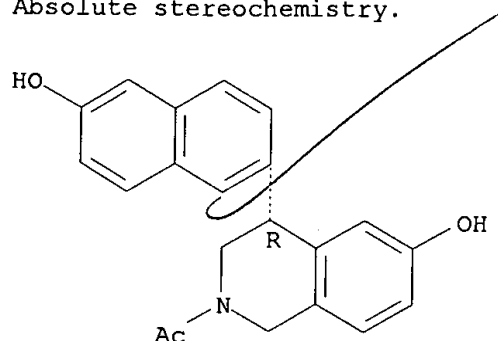
AB The unnatural alkaloid 6-methoxy-4-[2-(6-methoxy)naphthalenyl]-1,2,3,4-tetrahydroisoquinoline (I) was prepd. as a chiral spacer for optically active cyclophane receptors. Thus, intramol. cyclocondensation of formyl(methoxynaphthalenyl)phenylethylamine II gave the (methoxynaphthalenyl)dihydroisoquinoline which was reduced to I. II was prepd. in several steps from (6-methoxy-2-naphthyl) (3-methoxyphenyl)methanol. The S configuration was assigned by x-ray crystallog. methods to the hydrochloride salt of (-)-I. Starting from enantiomerically pure I, the optically active cyclophanes (R)- and (S)-III were prepd. These cyclophanes, in which the chiral alkaloid spacer is bridged to an achiral diphenylmethane unit, are efficient binders of naphthalene derivs. in D2O/CD3OD (60:40, vol./vol.) and show a modest degree of chiral recognition in the inclusion complexation of naproxen derivs.

IT 133043-20-6P 133043-31-9P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

09/704,306

(prepn. and alkylation of, with dichlorobutane)  
RN 133043-20-6 CAPLUS  
CN 6-Isoquinolinol, 2-acetyl-1,2,3,4-tetrahydro-4-(6-hydroxy-2-naphthalenyl)-  
, (R)- (9CI) (CA INDEX NAME)

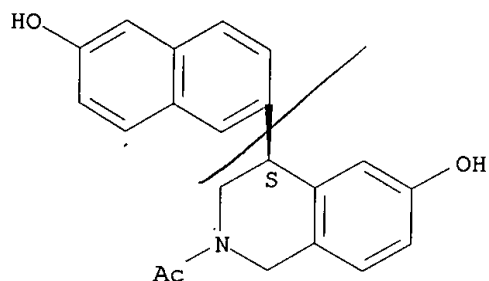
Absolute stereochemistry.



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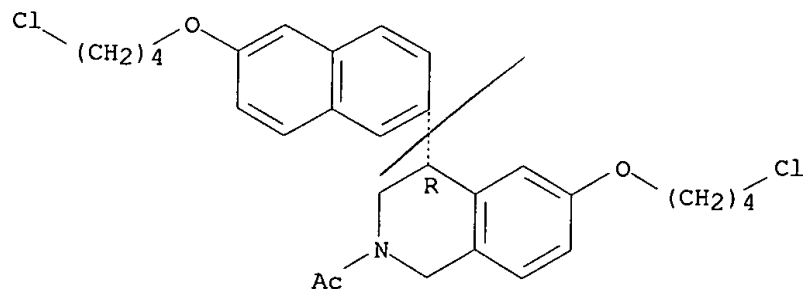
RN 133043-31-9 CAPLUS  
CN 6-Isoquinolinol, 2-acetyl-1,2,3,4-tetrahydro-4-(6-hydroxy-2-naphthalenyl)-  
, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 133043-21-7P 133043-22-8P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(prepn. and cyclization of, with bis(hydroxydimethylphenyl)piperidine)  
RN 133043-21-7 CAPLUS  
CN Isoquinoline, 2-acetyl-6-(4-chlorobutoxy)-4-[6-(4-chlorobutoxy)-2-  
naphthalenyl]-1,2,3,4-tetrahydro-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



Brenda Coleman

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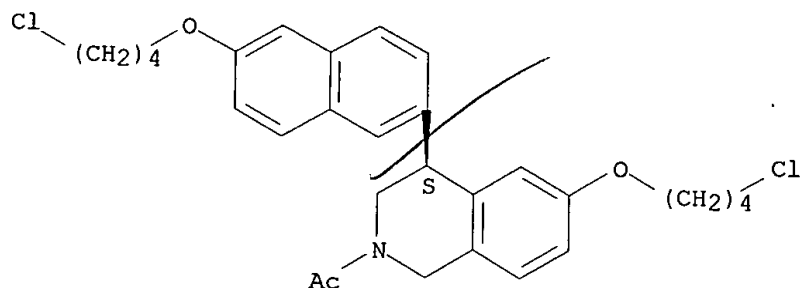


09/704,306

RN 133043-22-8 CAPLUS

CN Isoquinoline, 2-acetyl-6-(4-chlorobutoxy)-4-[6-(4-chlorobutoxy)-2-naphthalenyl]-1,2,3,4-tetrahydro-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



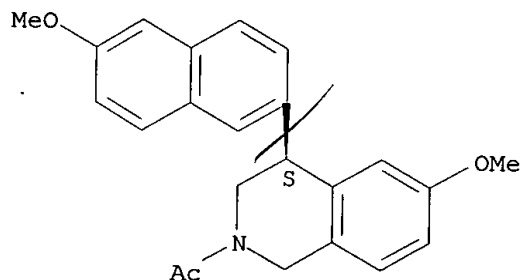
IT 133043-19-3P 133043-30-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (prepn. and demethylation of)

RN 133043-19-3 CAPLUS

CN Isoquinoline, 2-acetyl-1,2,3,4-tetrahydro-6-methoxy-4-(6-methoxy-2-naphthalenyl)-, (S)- (9CI) (CA INDEX NAME)

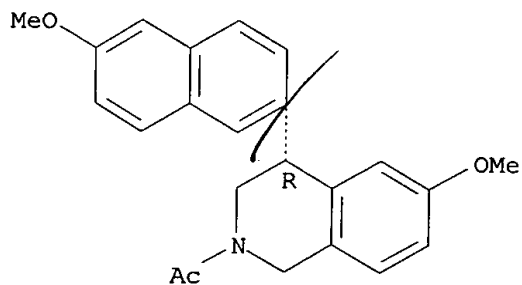
Absolute stereochemistry.



RN 133043-30-8 CAPLUS

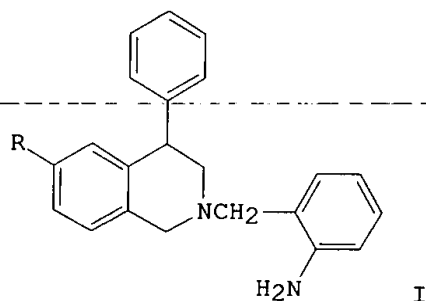
CN Isoquinoline, 2-acetyl-1,2,3,4-tetrahydro-6-methoxy-4-(6-methoxy-2-naphthalenyl)-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

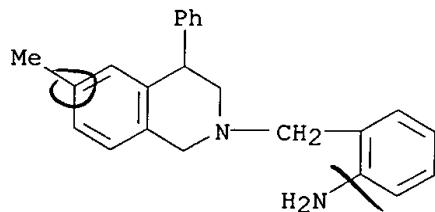


09/704,306

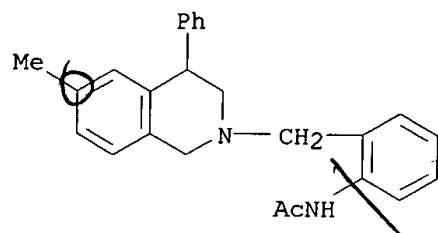
~~148~~ ANSWER 37 OF 100 CAPLUS COPYRIGHT 2003 ACS  
~~AN~~ 1991:185227 CAPLUS  
DN 114:185227  
TI Cyclization of N-(2-aminobenzyl)benzylamino-1-phenyl-1-ethanols and  
debenzylation of the resulting tetrahydroisoquinoline derivatives  
AU Zara-Kaczian, Erzsebet; Deak, Gyula; Szollosy, Aron; Brlik, Janos  
CS Inst. Exp. Med., Hung. Acad. Sci., Budapest, H-1450, Hung.  
SO Acta Chimica Hungarica (1990), 127(5), 743-55  
CODEN: ACHUDC; ISSN: 0231-3146  
DT Journal  
LA English  
OS CASREACT 114:185227  
GI



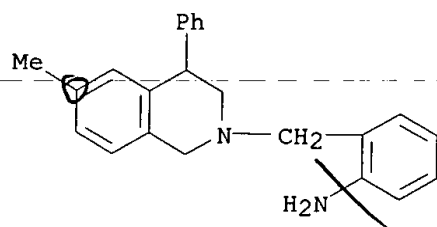
AB H<sub>2</sub>SO<sub>4</sub> treatment of 4-RC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>N(CH<sub>2</sub>C<sub>6</sub>H<sub>4</sub>NH<sub>2</sub>-2)CH<sub>2</sub>CH(OH)Ph (R = H, Me) gave  
tetrahydroquinolines I by intramol. cyclocondensation. I were  
debenzylation by catalytic hydrogenation or treatment with ClCO<sub>2</sub>Et.  
IT **133390-27-9P 133390-29-1P 133390-40-6P**  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(prepn. and debenzoylation of)  
RN 133390-27-9 CAPLUS  
CN Benzenamine, 2-[(3,4-dihydro-6-methyl-4-phenyl-2(1H)-isoquinolinyl)methyl]-  
(9CI) (CA INDEX NAME)



RN 133390-29-1 CAPLUS  
CN Acetamide, N-[2-[(3,4-dihydro-6-methyl-4-phenyl-2(1H)-  
isoquinolinyl)methyl]phenyl]- (9CI) (CA INDEX NAME)

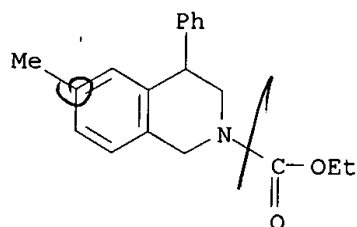


RN 133390-40-6 CAPLUS  
 CN Benzenamine, 2-[(3,4-dihydro-6-methyl-4-phenyl-2(1H)-isoquinolinyl)methyl]-, dihydrochloride (9CI) (CA INDEX NAME)



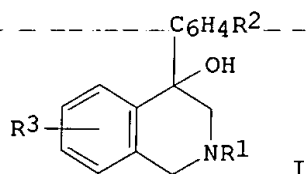
● 2 HCl

IT **133390-38-2P**  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 RN 133390-38-2 CAPLUS  
 CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-6-methyl-4-phenyl-, ethyl ester (9CI) (CA INDEX NAME)

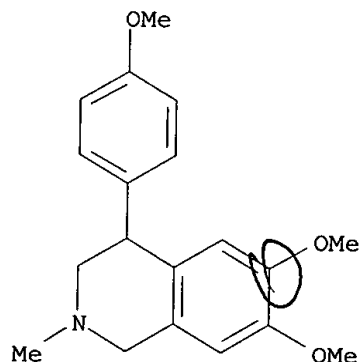


09/704,306

~~148~~ ANSWER 38 OF 100 CAPLUS COPYRIGHT 2003 ACS  
~~AN~~ 1991:43262 CAPLUS  
~~DN~~ 114:43262  
TI A new intramolecular Barbier reaction of N-(2-iodobenzyl)phenacylamines:  
a convenient synthesis of 1,2,3,4-tetrahydroisoquinolin-4-ols  
AU Kihara, Masaru; Kashimoto, Minoru; Kobayashi, Yoshimaro; Kobayashi,  
Shigeru  
CS Fac. Pharm. Sci., Univ. Tokushima, Tokushima, 770, Japan  
SO Tetrahedron Letters (1990), 31(37), 5347-8  
CODEN: TELEAY; ISSN: 0040-4039  
DT Journal  
LA English  
OS CASREACT 114:43262  
GI



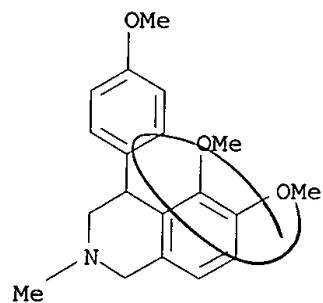
AB 4-Phenyl-1,2,3,4-tetrahydroisoquinolin-4-ols I [R1 = Me, R2 = R3 = H; R1 = Me, R2 = 4-MeO, R3 = H, 6,7-(MeO)2, 5,6-(MeO)2; R1 = CH2Ph, R1 = H, R2 = H, 6,7-(MeO)2; R1 = CO2Et R2 = R3 = H], potential Amaryllidaceae alkaloid intermediates, were prepd. by an intramol. Barbier reaction of N-(2-iodobenzyl)phenacylamines, R2C6H4COCH2NR1CH2C6H4R3I, with butyllithium in good yields.  
IT **66395-91-3P**, (.+-.)-O-Dimethylcherylline **115888-85-2P**, (.+-.)-O-Dimethylatifine  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of, via intramol. Barbier reaction)  
RN 66395-91-3 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-6,7-dimethoxy-4-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



RN 115888-85-2 CAPLUS

09/704,306

CN Isoquinoline, 1,2,3,4-tetrahydro-5,6-dimethoxy-4-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



L48 ANSWER 39 OF 100 CAPLUS COPYRIGHT 2003 ACS

AN 1990:565348 CAPLUS

DN 113:165348

TI Self-administration in baboons and the discriminative stimulus effects in rats of bupropion, nomifensine, diclofensine and imipramine

AU Lamb, R. J.; Griffiths, R.

CS Sch. Med., Johns Hopkins Univ., Baltimore, MD, 21225, USA

SO Psychopharmacology (Berlin, Germany) (1990), 102(2), 183-90

CODEN: PSCHDL; ISSN: 0033-3158

DT Journal

LA English

AB The behavioral effects of the antidepressants nomifensine, diclofensine, bupropion, and imipramine were examd. using a cocaine substitution drug self-administration procedure in baboons and a cocaine drug discrimination procedure in rats. I.v. self-administration of the antidepressants was examd. in baboons under conditions in which baseline responding was maintained by i.v. injections of cocaine HCl (0.32 mg/kg/injection). The antidepressants were substituted for cocaine for a period of 15 days, followed by a return to the cocaine baseline. Nomifensine, diclofensine, and bupropion maintained self-administration behavior at levels above those maintained by their resp. vehicles. Some doses of nomifensine, diclofensine, and bupropion maintained levels of behavior similar to those maintained under baseline cocaine conditions. High doses of imipramine maintained levels of behavior above those maintained by its vehicle, but the amt. of behavior maintained under these conditions was extremely small. Rats were trained to discriminate 32 .mu.mol cocaine/kg (i.p. 10 min before session) from no drug in a two-lever food reinforced drug discrimination procedure in which responding on one lever was reinforced following ten consecutive responses when the session was preceded by cocaine administration, while responding on the other lever was similarly reinforced in the absence of cocaine pretreatment. Cocaine, nomifensine, diclofensine, and bupropion caused dose-dependent cocaine-appropriate responding. Imipramine did not cause the cocaine-appropriate responding over a range of behaviorally active doses. The results are discussed in relation to the abuse potential of antidepressants.

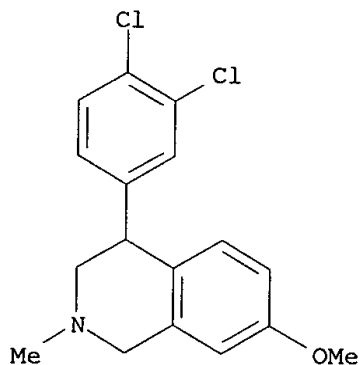
IT 67165-56-4, Diclofensine

RL: BIOL (Biological study)

(self-administration and discriminative behavior response to, abuse potential in relation to)

RN 67165-56-4 CAPLUS

CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-(9CI) (CA INDEX NAME)



~~L48~~ ANSWER 40 OF 100 CAPLUS COPYRIGHT 2003 ACS

AN 1990:515038 CAPLUS

DN 113:115038

TI 8-Amino-4-aryl-2-methyl-1,2,3,4-tetrahydroisoquinolines: reactions of the amino group via the diazonium salts. Synthesis and biological activity of novel 8-substituted 4-aryl-2-methyltetrahydroisoquinolines

AU Zara-Kaczian, Erzsebet; Deak, Gyula; Gyorgy, Lajos

CS Inst. Exp. Med., Hung. Acad. Sci., Budapest, H-1450, Hung.

SO Acta Chimica Hungarica (1989), 126(4), 573-84

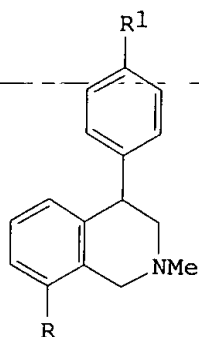
CODEN: ACHUDC; ISSN: 0231-3146

DT Journal

LA English

OS CASREACT 113:115038

GI



AB The amino group in isoquinoline deriv. I (R = H<sub>2</sub>N; R<sub>1</sub> = H, Cl) was exchanged for other groups via the diazonium salt: to give I (R = F, O<sub>2</sub>N, Cl, HO, N<sub>3</sub>). I inhibited haloperidol-induced catalepsy, tetrabenazine-induced ptosis, and reserpine-induced hypothermia; the dopaminomimetic and antidepressant mol. structure activity relationship was investigated.

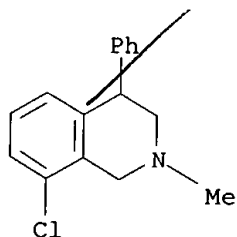
IT 118411-63-5P 118411-64-6P 129010-56-6P  
129010-59-9P 129010-60-2P 129010-61-3P  
129010-74-8P 129010-75-9P 129010-76-0P  
129010-79-3P 129010-80-6P 129010-81-7P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. and dopaminomimetic and antidepressant activity of)

RN 118411-63-5 CAPLUS

CN Isoquinoline, 8-chloro-1,2,3,4-tetrahydro-2-methyl-4-phenyl- (9CI) (CA INDEX NAME)



09/704,306

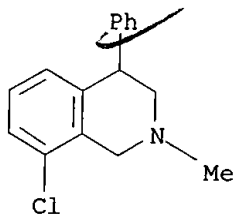
RN 118411-64-6 CAPLUS

CN Isoquinoline, 8-chloro-1,2,3,4-tetrahydro-2-methyl-4-phenyl-,  
(2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 118411-63-5

CMF C16 H16 Cl N

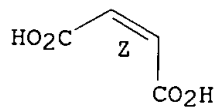


CM 2

CRN 110-16-7

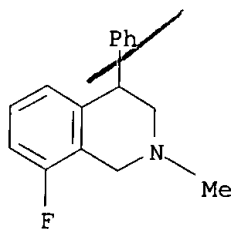
CMF C4 H4 O4

Double bond geometry as shown.



RN 129010-56-6 CAPLUS

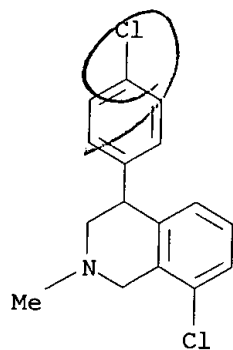
CN Isoquinoline, 8-fluoro-1,2,3,4-tetrahydro-2-methyl-4-phenyl- (9CI) (CA  
INDEX NAME)



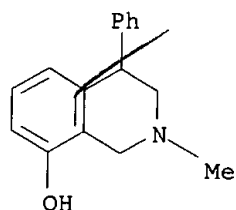
RN 129010-59-9 CAPLUS

CN Isoquinoline, 8-chloro-4-(4-chlorophenyl)-1,2,3,4-tetrahydro-2-methyl-  
(9CI) (CA INDEX NAME)

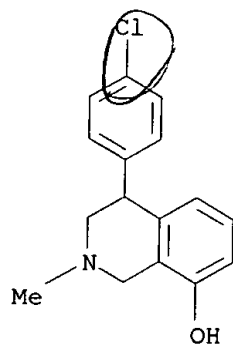




RN 129010-60-2 CAPLUS  
CN 8-Isoquinolinol, 1,2,3,4-tetrahydro-2-methyl-4-phenyl- (9CI) (CA INDEX NAME)



RN 129010-61-3 CAPLUS  
CN 8-Isoquinolinol, 4-(4-chlorophenyl)-1,2,3,4-tetrahydro-2-methyl- (9CI) (CA INDEX NAME)

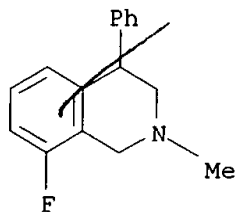


RN 129010-74-8 CAPLUS  
CN Isoquinoline, 8-fluoro-1,2,3,4-tetrahydro-2-methyl-4-phenyl-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 129010-56-6  
CMF C16 H16 F N

09/704,306

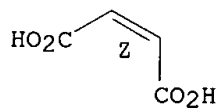


CM 2

CRN 110-16-7

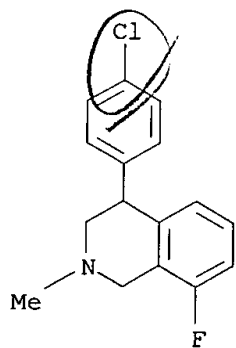
CMF C4 H4 O4

Double bond geometry as shown.



RN 129010-75-9 CAPLUS

CN Isoquinoline, 4-(4-chlorophenyl)-8-fluoro-1,2,3,4-tetrahydro-2-methyl-  
(9CI) (CA INDEX NAME)



RN 129010-76-0 CAPLUS

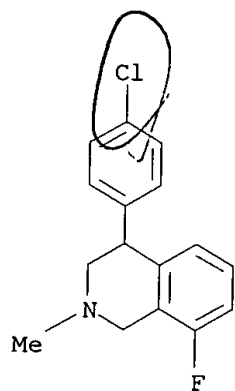
CN Isoquinoline, 4-(4-chlorophenyl)-8-fluoro-1,2,3,4-tetrahydro-2-methyl-,  
(2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 129010-75-9

CMF C16 H15 Cl F N

09/704,306

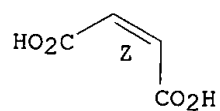


CM 2

CRN 110-16-7

CMF C4 H4 O4

Double bond geometry as shown.



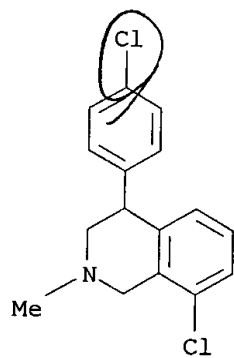
RN 129010-79-3 CAPLUS

CN Isoquinoline, 8-chloro-4-(4-chlorophenyl)-1,2,3,4-tetrahydro-2-methyl-,  
(2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 129010-59-9

CMF C16 H15 Cl2 N



CM 2

CRN 110-16-7

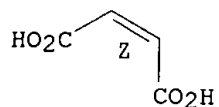
CMF C4 H4 O4

Brenda Coleman

<page

09/704,306

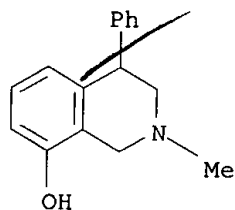
Double bond geometry as shown.



RN 129010-80-6 CAPLUS  
CN 8-Isoquinolinol, 1,2,3,4-tetrahydro-2-methyl-4-phenyl-,  
(2Z)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

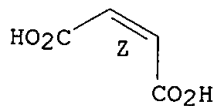
CRN 129010-60-2  
CMF C16 H17 N O



CM 2

CRN 110-16-7  
CMF C4 H4 O4

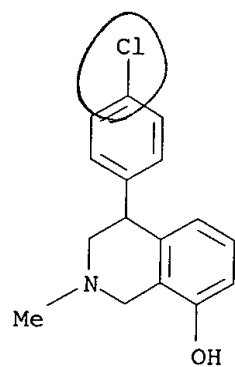
Double bond geometry as shown.



RN 129010-81-7 CAPLUS  
CN 8-Isoquinolinol, 4-(4-chlorophenyl)-1,2,3,4-tetrahydro-2-methyl-,  
(2Z)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 129010-61-3  
CMF C16 H16 Cl N O

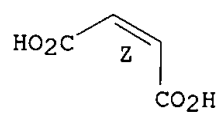


CM 2

CRN 110-16-7

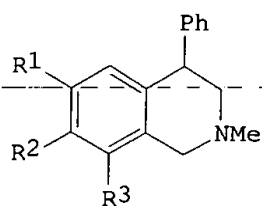
CMF C4 H4 O4

Double bond geometry as shown.



09/704,306

~~148~~ ANSWER 41 OF 100 CAPLUS COPYRIGHT 2003 ACS  
~~AN~~ 1990:497422 CAPLUS  
~~DN~~ 113:97422  
TI A new synthesis of 1,2,3,4-tetrahydro-2-methyl-4-phenylisoquinolines  
AU Venkov, A.; Vodenicharov, D.  
CS Dep. Chem., Univ. Plovdiv, Plovdiv, 4000, Bulg.  
SO Synthesis (1990), (3), 253-5  
CODEN: SYNTBF; ISSN: 0039-7881  
DT Journal  
LA English  
OS CASREACT 113:97422  
GI

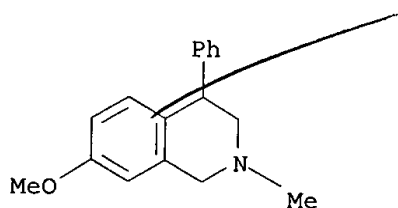


AB 1,2,3,4-Tetrahydro-2-methyl-4-phenylisoquinolines I (R1 = R2 = OMe, R3 = H; R1 = OH, R2 = OMe, R3 = H; R1 = H, R2 = R3 = OMe; R1 = R3 = H, R2 = OMe; R1 = OMe, R2 = R3 = H; R1 = R2 = H, R3 = H, NH2; R1R2 = OCH2O, R3 = H) are obtained from arom. aldehydes R1R2R3C6H2CHO, MeNH2, and .alpha.-haloacetophenones in the presence of NaBH4 followed by cyclization with H2SO4 and Zn in MeOH.

IT 37624-27-4P 59645-78-2P 88776-67-4P  
128942-65-4P 128942-66-5P 128942-68-7P  
128942-70-1P 128942-72-3P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

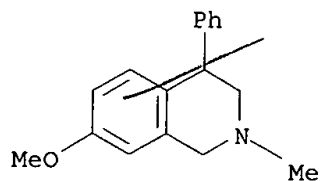
RN 37624-27-4 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-phenyl-, hydrochloride (9CI) (CA INDEX NAME)

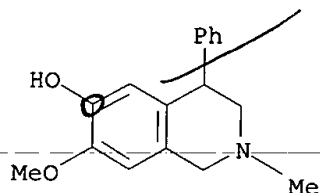


RN 59645-78-2 CAPLUS

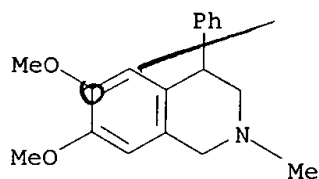
CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-phenyl- (9CI) (CA INDEX NAME)



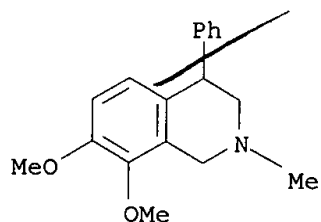
RN 88776-67-4 CAPLUS  
CN 6-Isoquinolinol, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-phenyl- (9CI)  
(CA INDEX NAME)



RN 128942-65-4 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-6,7-dimethoxy-2-methyl-4-phenyl- (9CI)  
(CA INDEX NAME)

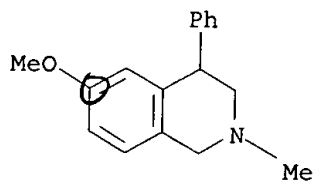


RN 128942-66-5 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-7,8-dimethoxy-2-methyl-4-phenyl- (9CI)  
(CA INDEX NAME)



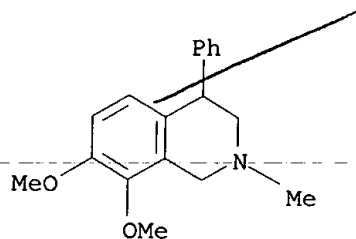
RN 128942-68-7 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-6-methoxy-2-methyl-4-phenyl- (9CI) (CA  
INDEX NAME)

09/704,306



RN 128942-70-1 CAPLUS

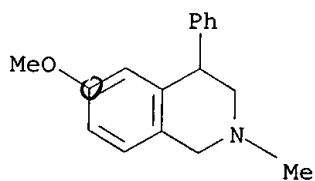
CN Isoquinoline, 1,2,3,4-tetrahydro-7,8-dimethoxy-2-methyl-4-phenyl-,  
hydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 128942-72-3 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-6-methoxy-2-methyl-4-phenyl-,  
hydrochloride (9CI) (CA INDEX NAME)



● HCl



09/704,306

~~148~~ ANSWER 42 OF 100 CAPLUS COPYRIGHT 2003 ACS

~~AN~~ 1990:478123 CAPLUS

~~DN~~ 113:78123

~~TI~~ Increasing 5-lipoxygenase inhibitory activities by oxidative conversion of o-methoxyphenols to catechols using a copper-ascorbic acid-oxygen system

~~AU~~ Aihara, Kazuhiro; Higuchi, Tsunehiko; Hirobe, Masaaki

~~CS~~ Fac. Pharm. Sci., Univ. Tokyo, Tokyo, 113, Japan

~~SO~~ Chemical & Pharmaceutical Bulletin (1990), 38(3), 842-4

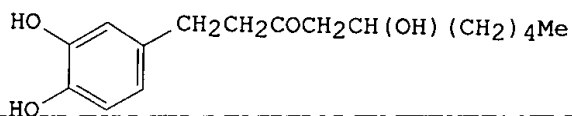
CODEN: CPBTAL; ISSN: 0009-2363

~~DT~~ Journal

~~LA~~ English

~~OS~~ CASREACT 113:78123

~~GI~~



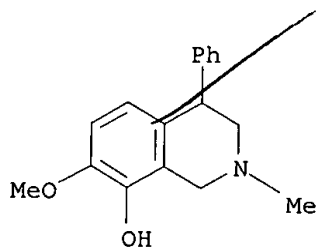
AB Several complicated o-methoxyphenols were oxidized with high selectivity to catechols by a Cu<sup>2+</sup>-ascorbic acid-O<sub>2</sub> system. In this way, the 5-lipoxygenase inhibitory activities of o-methoxyphenols were greatly increased. [6]-Norigingerol (I) derived from [6]-gingerol, shows promise as a lead compd. for new drugs because of its high inhibitory potency (IC<sub>50</sub> = 5.0 .times. 10<sup>-8</sup> M).

IT **88776-68-5**

RL: RCT (Reactant); RACT (Reactant or reagent)  
(oxidn. of, catechol deriv. from)

RN 88776-68-5 CAPLUS

CN 8-Isoquinolinol, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-phenyl- (9CI)  
(CA INDEX NAME)



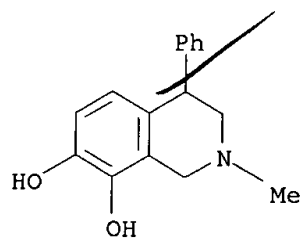
IT **128670-71-3P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 128670-71-3 CAPLUS

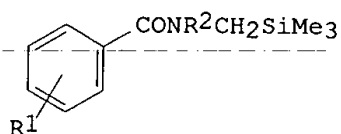
CN 7,8-Isoquinolinediol, 1,2,3,4-tetrahydro-2-methyl-4-phenyl- (9CI) (CA INDEX NAME)

09/704,306



09/704,306

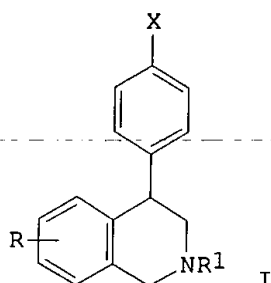
~~LA~~ ANSWER 43 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1990:423645 CAPLUS  
DN 113:23645  
TI .alpha.'-Silylated tertiary benzamides as dual ortho-and  
.alpha.'-carbanion synthons. Carbodesilylative routes to isoquinoline and  
dibenzoquinolizidine derivatives  
AU Cuevas, J. C.; Snieckus, V.  
CS Guleph-Waterloo Cent. Grad. Work Chem., Univ. Waterloo, Waterloo, ON, N2L  
3G1, Can.  
SO Tetrahedron Letters (1989), 30(43), 5837-40  
CODEN: TELEAY; ISSN: 0040-4039  
DT Journal  
LA English  
OS CASREACT 113:23645  
GI



AB .alpha.'-Silylated benzamides I (R1 = H, 3-MeO, 4-MeO, 2-Ph, 2-MeO, 2-Cl,  
etc) display both ortho- and .alpha.'-carbanion reactivities which are  
translated into new synthetic routes for isoquinoline and protoberberine  
derivs.  
IT **110841-21-9P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)  
RN 110841-21-9 CAPLUS

09/704,306

~~DI~~ 8 ANSWER 44 OF 100 CAPLUS COPYRIGHT 2003 ACS  
~~AN~~ 1990:422965 CAPLUS  
DN 113:22965  
TI Acid-base behavior of a series of 4-phenyl-1,2,3,4-tetrahydroisoquinolines  
- experimental determination and theoretical calculation  
AU Doichinova, I.; Mikhailova, D.; Nacheva, R.  
CS Nauchen Inst. Farmakol. Farm., MA, Bulg.  
SO Farmatsiya (Sofia, Bulgaria) (1989), 39(6), 4-8  
CODEN: FMTYA2; ISSN: 0428-0296  
DT Journal  
LA Bulgarian  
GI

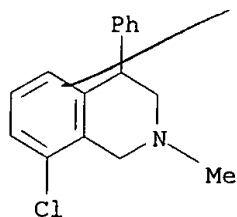


AB Exptl. pKa values were detd. for 14 title compds. I [R = H, 8-H<sub>2</sub>N, 8-EtO<sub>2</sub>CNH, 8-Cl, 6,7-(MeO)<sub>2</sub>; R<sub>1</sub> = Me, CH<sub>2</sub>CHPhOH, CH<sub>2</sub>COPh; X = H, F, Cl, Br] in 50, 70, and 90% aq. EtOH and extrapolated for aq. soln. A Taft equation was derived from this data. R and X had little effect on I protonation, but I basicity decreased in the stated order of R<sub>1</sub>. The effect of solvent polarity on the acid-base equil. of I increased in the stated order of R<sub>1</sub>.

IT 118411-63-5 127513-46-6 127562-98-5  
127562-99-6 127563-00-2 127563-01-3  
127770-47-2  
RL: PRP (Properties)  
(acid-base properties of)

RN 118411-63-5 CAPLUS

CN Isoquinoline, 8-chloro-1,2,3,4-tetrahydro-2-methyl-4-phenyl- (9CI) (CA INDEX NAME)

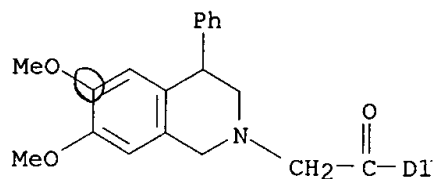


RN 127513-46-6 CAPLUS

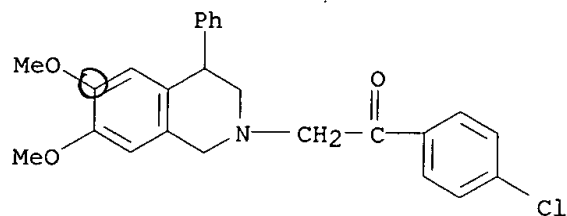
CN Ethanone, 2-(3,4-dihydro-6,7-dimethoxy-4-phenyl-2(1H)-isoquinolinyl)-1-(dimethoxyphenyl)- (9CI) (CA INDEX NAME)



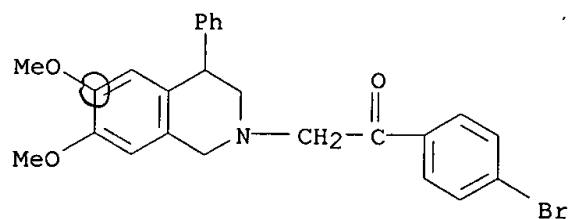
2 ( D1-O-Me )



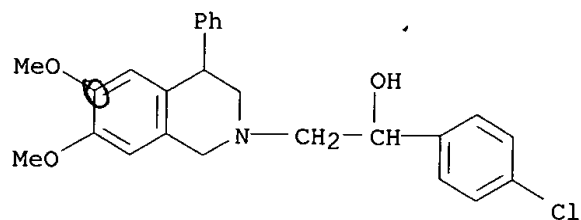
RN 127562-98-5 CAPLUS  
CN Ethanone, 1-(4-chlorophenyl)-2-(3,4-dihydro-6,7-dimethoxy-4-phenyl-2(1H)-isoquinolinyl)- (9CI) (CA INDEX NAME)



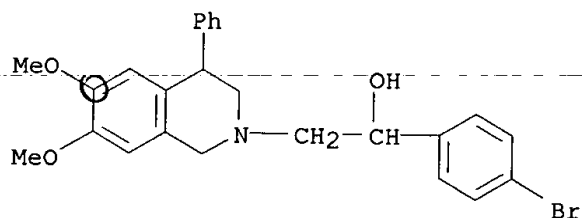
RN 127562-99-6 CAPLUS  
CN Ethanone, 1-(4-bromophenyl)-2-(3,4-dihydro-6,7-dimethoxy-4-phenyl-2(1H)-isoquinolinyl)- (9CI) (CA INDEX NAME)



RN 127563-00-2 CAPLUS  
CN 2(1H)-Isoquinolineethanol, .alpha.-(4-chlorophenyl)-3,4-dihydro-6,7-dimethoxy-4-phenyl- (9CI) (CA INDEX NAME)



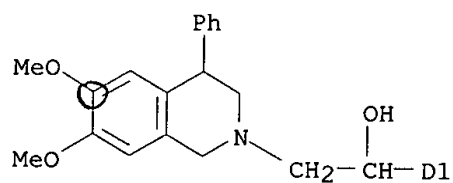
RN 127563-01-3 CAPLUS  
 CN 2(1H)-Isoquinolineethanol, .alpha.-(4-bromophenyl)-3,4-dihydro-6,7-dimethoxy-4-phenyl- (9CI) (CA INDEX NAME)



RN 127770-47-2 CAPLUS  
 CN 2(1H)-Isoquinolineethanol, .alpha.-(dimethoxyphenyl)-3,4-dihydro-6,7-dimethoxy-4-phenyl- (9CI) (CA INDEX NAME)

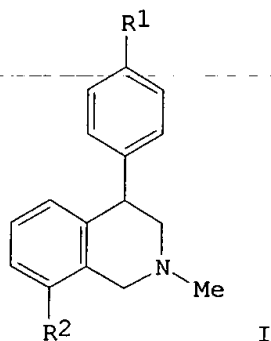


2 ( D1-O-Me )



09/704,306

~~L48~~ ANSWER 45 OF 100 CAPLUS COPYRIGHT 2003 ACS  
~~AN~~ 1990:406131 CAPLUS  
DN 113:6131  
TI Synthesis, stereochemistry, and antiulcer activity of 4-phenyltetrahydroisoquinolines  
AU Ivanova, N.; Ivanov, Ch.; Mondeshka, D.; Berova, N.; Angelova, I.; Rakovska, R.; Boyadzhiev, S.; Tancheva, Ch.; Tasheva, D.  
CS Chem.-Pharm. Comb., Sofia, 1220, Bulg.  
SO Archiv der Pharmazie (Weinheim, Germany) (1990), 323(1), 3-7  
CODEN: ARPMAS; ISSN: 0365-6233  
DT Journal  
LA German  
OS CASREACT 113:6131  
GI



AB Racemic and optically active tetrahydroisoquinolines I (R1 = H, Cl; R2 = NHCO2Et, NH2, Cl) were prepd. and tested for their gastric ulcer-inhibiting activity in rats. The antiulcer activity of (.+.)-I (R1 = Cl, R2 = NHCO2Et) (II) was 30-50 times higher than that of cimetidine or ranitidine; (S)-(+)-II was 3 times as active as (R)-(-)-II. I (R1 = H, R2 = NHCO2Et), II and I (R1 = Cl, R2 = NH2) had antidepressant activity and inhibited noradrenalin and dopamine uptake.

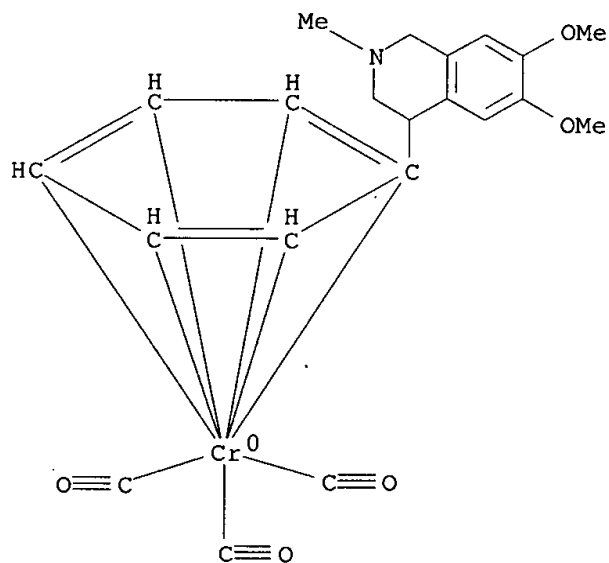
IT **125786-24-5P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and dehalogenation and gastric ulcer-inhibiting activity of)

RN 125786-24-5 CAPLUS

IT **127441-86-5P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and gastric ulcer-inhibiting activity of)

RN 127441-86-5 CAPLUS

48 ANSWER 46 OF 100 CAPLUS COPYRIGHT 2003 ACS  
 AN 1990:235140 CAPLUS  
 DN 112:235140  
 TI Enantiospecific synthesis of (+)-(R)-6,7-dimethoxy-2-methyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline from (+)-(S)-2-methylamino-1-phenylethanol  
 AU Coote, Steven J.; Davies, Stephen G.; Middlemiss, David; Naylor, Alan  
 CS Dyson Perrins Lab., Univ. Oxford, Oxford, OX1 3QY, UK  
 SO Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1989), (12), 2223-8  
 CODEN: JCPRB4; ISSN: 0300-922X  
 DT Journal  
 LA English  
 OS CASREACT 112:235140  
 AB Acid-promoted cyclization of (+)-(R)-N-(3,4-dimethoxybenzyl)halostachine tricarboxylchromium at -20.degree. is highly stereoselective proceeding with retention of configuration to yield, after removal of the tricarboxylchromium unit, homochiral (+)-(R)-6,7-dimethoxy-2-methyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline. In contrast, cyclization of (-)-(R)-N-(3,4-dimethoxybenzyl)halostachine under acidic conditions at -20.degree. showed poor stereoselectivity giving predominantly the tetrahydroisoquinoline product corresponding to inversion of configuration, (+)-(R)-6,7-dimethoxy-2-methyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline, with an enantiomeric excess of 54%.  
 IT **127306-58-5P**  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (prepn. and cyclization of, isoquinoline deriv. from)  
 RN 127306-58-5 CAPLUS  
 IT **127261-39-6P**  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (prepn. and oxidn. of)  
 RN 127261-39-6 CAPLUS  
 CN Chromium, tricarboxyl[1,2,3,4-tetrahydro-6,7-dimethoxy-2-methyl-4-(.eta.6-phenyl)isoquinoline]-, stereoisomer (9CI) (CA INDEX NAME)





09/704,306

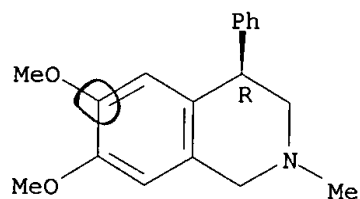
IT 127239-57-0P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 127239-57-0 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-6,7-dimethoxy-2-methyl-4-phenyl-, (R)-  
(9CI) (CA INDEX NAME)

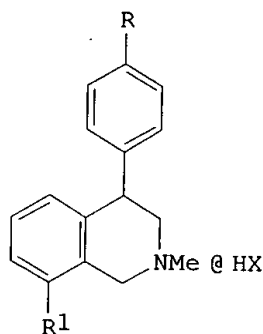
Absolute stereochemistry.



09/704,306

ANSWER 47 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1990:132480 CAPLUS  
DN 112:132480  
TI Preparation of 4-phenyl-1,2,3,4-tetrahydroisoquinolines as ulcer inhibitors  
IN Ivanov, Ch.; Ivanova, N.; Paskov, V.; Daleva, L.; Mondeshka, D.; Berova, N.; Rakovska, R.; Tosheva, D.; Zaikov, Kh.; et al.  
PA "Farmakhim" State Enterprises, Sofia, UK  
SO Eur. Pat. Appl., 15 pp.  
CODEN: EPXXDW  
DT Patent  
LA German  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 314828	A1	19890510	EP 1987-116188	19871103
	EP 314828	B1	19910529		
	R: BE, CH, DE, ES, FR, GB, LI, NL, SE				
	ES 2038646	T3	19930801	ES 1987-116188	19871103
	SU-1836951	A1	19930830	SU 1987-7774635	19871116
PRAI	EP 1987-116188		19871103		
OS	MARPAT 112:132480				
GI					

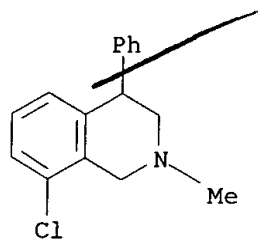


AB The title compds. I (R = H, halo; R1 = halo, NH2, NHCO2Et; X = halo, HOCOCH:CHCO2H) are prepd. as ulcer inhibition. N-(2-Chlorobenzyl)-1-phenyl-2-methylaminoethanol (prepn. given) was cyclized with H2SO4, in CH2Cl2, to give 2-methyl-4-phenyl-8-chloro-1,2,3,4-tetrahydroisoquinoline, which was subjected to optical resoln. with (-)-2R,3R-O,O-di(p-toluy) tartrate. Oral administration of I (R = Cl, R1 = NHCO2Et) (free base), at 1 mg/kg, prevented the development of water-immersion ulcer, in rats.

IT **118411-63-5P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and optical resoln. of)

RN 118411-63-5 CAPLUS

CN Isoquinoline, 8-chloro-1,2,3,4-tetrahydro-2-methyl-4-phenyl- (9CI) (CA INDEX NAME)



IT 125786-24-5P 125786-28-9P 125786-29-0P

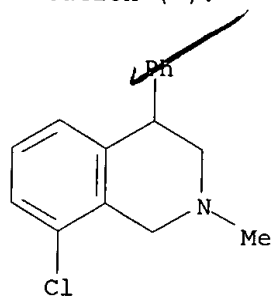
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of, as ulcer inhibitor)

RN 125786-24-5 CAPLUS

RN 125786-28-9 CAPLUS

CN Isoquinoline, 8-chloro-1,2,3,4-tetrahydro-2-methyl-4-phenyl-, (-)- (9CI)  
(CA INDEX NAME)

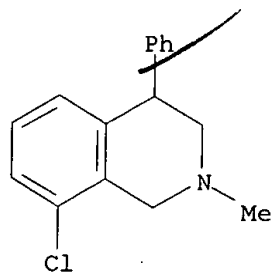
-----Rotation (-).-----



RN 125786-29-0 CAPLUS

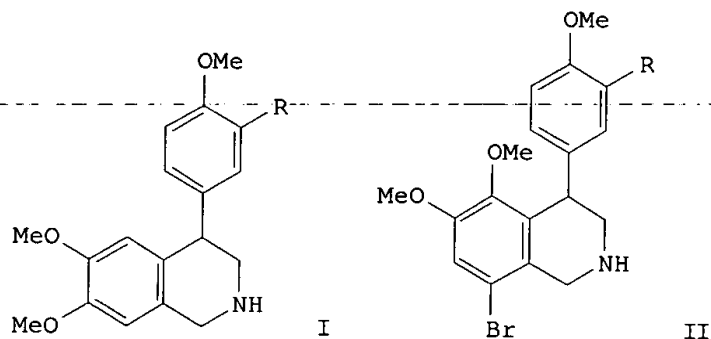
CN Isoquinoline, 8-chloro-1,2,3,4-tetrahydro-2-methyl-4-phenyl-, (+)- (9CI)  
(CA INDEX NAME)

Rotation (+).

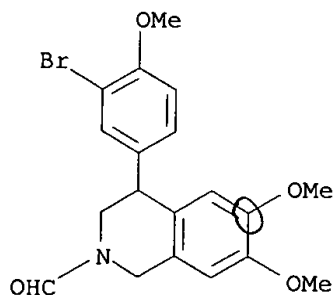


09/704,306

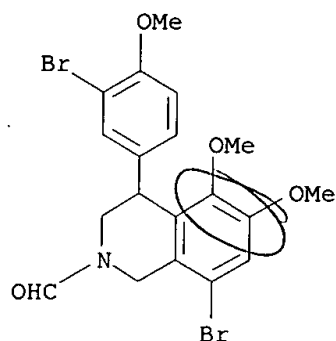
~~L48~~ ANSWER 48 OF 100 CAPLUS COPYRIGHT 2003 ACS  
~~AM~~ 1990:77652 CAPLUS  
DN 112:77652  
TI A one-pot formation of the analogs of cherylline- and latifine-type  
4-aryl-1,2,3,4-tetrahydroisoquinolines  
AU Kihara, Masaru; Iguchi, Seiichiro; Imakura, Yasuhiro; Kobayashi, Shigeru  
CS Fac. Pharm. Sci., Univ. Tokushima, Tokushima, 770, Japan  
SO Heterocycles (1989), 29(6), 1097-105  
CODEN: HTCYAM; ISSN: 0385-5414  
DT Journal  
LA English  
OS CASREACT 112:77652  
GI



AB The cyclization reaction of N-(2-bromo-4,5-dimethoxybenzyl)-1-(4-methoxyphenyl)-2-aminoethanol with conc. H<sub>2</sub>SO<sub>4</sub>, 80% H<sub>2</sub>SO<sub>4</sub>, or conc. HCl-benzene yielded cherylline analogs I (R = Br, H) along with latifine analogs II (R = H, Br) according to the biogenetic route.  
IT **125140-42-3P 125140-43-4P**  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and redn. of)  
RN 125140-42-3 CAPLUS  
CN 2(1H)-Isoquinolinecarboxaldehyde, 4-(3-bromo-4-methoxyphenyl)-3,4-dihydro-6,7-dimethoxy- (9CI) (CA INDEX NAME)



RN 125140-43-4 CAPLUS  
CN 2(1H)-Isoquinolinecarboxaldehyde, 8-bromo-4-(3-bromo-4-methoxyphenyl)-3,4-dihydro-5,6-dimethoxy- (9CI) (CA INDEX NAME)

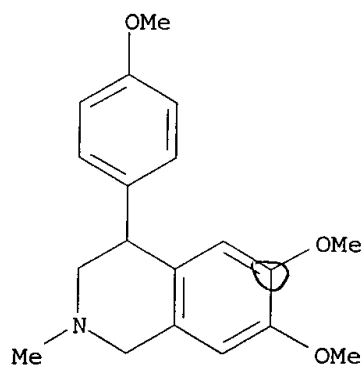


IT **66395-91-3P**, (.+-.)-O,O-Dimethylcherylline **115888-85-2P**,  
(.+-.)-O,O-Dimethylatifine

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

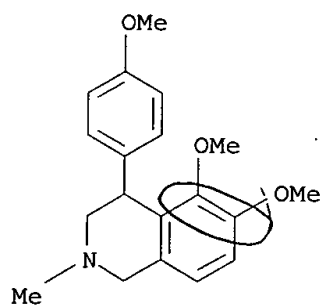
RN 66395-91-3 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-6,7-dimethoxy-4-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



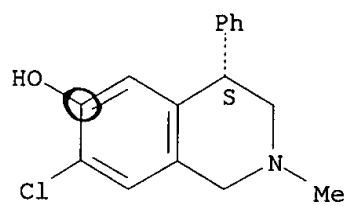
RN 115888-85-2 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-5,6-dimethoxy-4-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



148 ANSWER 49 OF 100 CAPLUS COPYRIGHT 2003 ACS  
 AN 1989:508484 CAPLUS  
 DN 111:108484  
 TI Conformational analysis and molecular modeling of 1-phenyl-, 4-phenyl-,  
 and 1-benzyl-1,2,3,4-tetrahydroisoquinolines as D1 dopamine receptor  
 ligands  
 AU Charifson, Paul S.; Bowen, J. Phillip; Wyrick, Steven D.; Hoffman, Andrew  
 J.; Cory, Michael; McPhail, Andrew T.; Mailman, Richard B.  
 CS Sch. Pharm., Univ. North Carolina, Chapel Hill, NC, 27599-7360, USA  
 SO Journal of Medicinal Chemistry (1989), 32(9), 2050-8  
 CODEN: JMCMAR; ISSN: 0022-2623  
 DT Journal  
 LA English  
 AB Conformational studies on a series of 1-phenyl-, 4-phenyl-, and  
 1-benzyl-1,2,3,4-tetrahydroisoquinolines that possess an identical  
 substituent pattern to the prototypical D1 dopamine receptor antagonist  
 SCH23390 [(R)-(+)-7-chloro-8-hydroxy-3-methyl-1-phenyl-2,3,4,5-tetrahydro-  
 1H-3-benzazepine (I)] were performed with use of mol. mechanics calcns.  
 (MM2(85), with newly developed arom. halide bending and torsional  
 parameters that are now incorporated into MM2(87)), single-crystal x-ray  
 anal., and high-field NMR spectroscopy. The synthesis and biol. testing  
 of these compds. have been previously reported. The test compds. were  
 compared both quant. and graphically to I. Calcns. on both the free-base  
 and protonated forms of each compd. were carried out. To ensure that  
 conformation space was adequately sampled, the test compds. were energy  
 minimized from different starting geometries; ring inversion of the  
 heterocycle was employed, as were dihedral driver calcns. on the Ph or  
 benzyl rings. For N-methyl-6-chloro-7-hydroxy-1-phenyl-1,2,3,4-  
 tetrahydroisoquinoline (II), the torsion angle .tau.(C8a-C1-C12-C17) had  
 energy min. at .apprx.60 and 240.degree.. This finding was corroborated  
 by NMR studies that indicated a dramatic upfield chem. shift of ArH8 after  
 ring cyclization. The N lone pair or H vector was approx. orthogonal to  
 the plane of the substituted arom. ring in the tetrahydroisoquinolines;  
 this explained the upfield chem. shift of the vicinal chiral proton (H1).  
 In all instances, the 6-membered heterocyclic ring in the energy-minimized  
 structures preferred the half-chair conformation with the Ph rings  
 pseudo-equatorial. Distance comparisons of the proposed pharmacophoric  
 atoms (Cl, N, O, centroid of the Ph or benzyl ring) showed that the Ph or  
 benzyl centroid to ammonium H distance, Cl to N distance, and distance of  
 the N above or below the plane of the isoquinoline arom. ring were the  
 distances most highly correlated with biol. activity. Resoln. and  
 single-crystal x-ray anal. of II showed the most active enantiomer to  
 possess the S abs. configuration, in contrast to the benzazepine (R)-I.  
 Least-squares fitting of the energy-minimized structures with SYBYL mol.  
 modeling software showed that (S)-(+)-II, rather than (R)-(-)-II, gave a  
 better fit to (R)-I. Vol. detns. derived from SYBYL multifit analyses  
 aided in receptor mapping to qual. describe areas of "active"  
 pharmacophore space as well as areas of "inactive" substituent space. A  
 correlation (r = 0.95) was found relating the calcd. dipole moment  
 orientations with D1 receptor binding affinity.  
 IT 121959-74-8  
 RL: BIOL (Biological study)  
 (dopaminergic D1 antagonism by, structure in relation to)  
 RN 121959-74-8 CAPLUS  
 CN 6-Isoquinolinol, 7-chloro-1,2,3,4-tetrahydro-2-methyl-4-phenyl-, (S)-  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L48 ANSWER 50 OF 100 CAPLUS COPYRIGHT 2003 ACS

AN 1989:470227 CAPLUS

DN 111:70227

TI 1-Anilinonaphthalene-8-sulfonic acid (ANS) as a probe for the binding of antidepressant drugs to human .alpha.1-acid glycoprotein (AAG)

AU Zini, R.; Copigneaux, C.; Tillement, J. P.

CS Dep. Pharmacol., Fac. Med., Creteil, 94010, Fr.

SO Progress in Clinical and Biological Research (1989), Volume Date 1988, 300(Alpha-Acid Glycoprotein), 417-21  
CODEN: PCBRD2; ISSN: 0361-7742

DT Journal

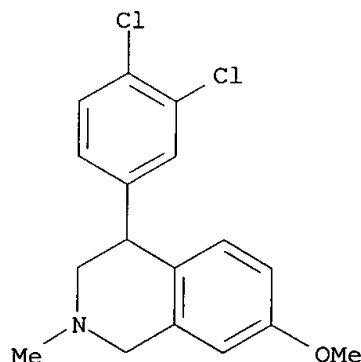
LA English

AB The fluorescent dye ANS exhibits an intense increase in fluorescence after binding to human AAG, allowing it to be used as a fluorescent probe with which to study the binding of AAG to drugs such as antidepressants. ANS binding to AAG is inhibited by many drugs, binedaline being the most potent inhibitor studied. Apparently, all antidepressants share the same binding site on AAG. Fluorescence spectroscopy employing ANS has been used to det. the  $K_i$  values of 34 antidepressants.-----  
IT 67165-56-4, Diclofensine

RL: BIOL (Biological study)

(binding of, to human .alpha.1-acid glycoprotein,  
anilinonaphthalenesulfonic acid as fluorescent probe for study of)

RN 67165-56-4 CAPLUS

CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-  
(9CI) (CA INDEX NAME)



09/704,306

~~LE~~ ANSWER 51 OF 100 CAPLUS COPYRIGHT 2003 ACS

AN 1989:95022 CAPLUS

DN 110:95022

TI Preparation of heterobicyclic compounds as nephrovascular tract dilators

IN Tanaka, Akihiro; Fujikura, Takashi; Tsuzuki, Ryuji; Yokota, Masaki; Yatsu, Takeyuki

PA Yamanouchi Pharmaceutical Co., Ltd., Japan

SO Eur. Pat. Appl., 40 pp.

CODEN: EPXXDW

DT Patent

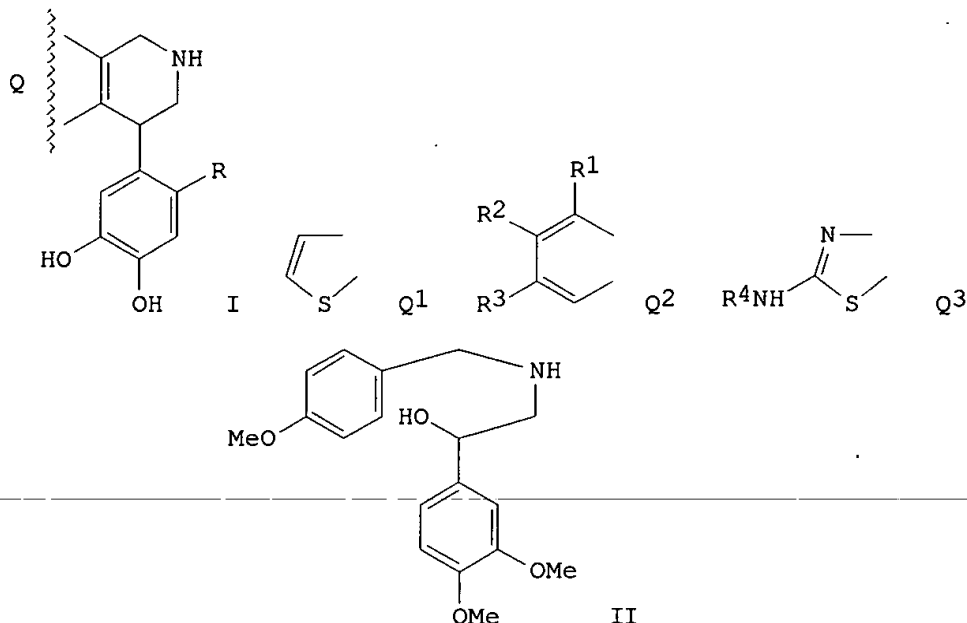
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 286293	A1	19881012	EP 1988-302757	19880328
	EP 286293	B1	19920701		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	JP 01199948	A2	19890811	JP 1988-70125	19880323
	JP 05075745	B4	19931021		
	US 4876261	A	19891024	US 1988-173376	19880325
	EP 399626	A2	19901128	EP 1990-201982	19880328
	EP 399626	A3	19901205		
	EP 399626	B1	19950607		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	AT 77820	E	19920715	AT 1988-302757	19880328
	ES 2041790	T3	19931201	ES 1988-302757	19880328
	ES 2075137	T3	19951001	ES 1990-201982	19880328
	US 4966904	A	19901030	US 1989-320975	19890309
	US 5079256	A	19920107	US 1989-412840	19890926
	US 5077406	A	19911231	US 1990-518579	19900503
	US 5204468	A	19930420	US 1991-737883	19910725
	US 5378849	A	19950103	US 1992-981137	19921124
	US 5623074	A	19970422	US 1994-269733	19940630
PRAI	JP 1987-75439		19870327		
	JP 1987-129368		19870525		
	JP 1987-200562		19870810		
	JP 1987-200563		19870810		
	JP 1987-226184		19870909		
	JP 1987-227398		19870910		
	JP 1987-247590		19870929		
	JP 1987-254012		19871007		
	US 1988-173276		19880325		
	US 1988-173376		19880325		
	EP 1988-302757		19880328		
	US 1989-320975		19890309		
	US 1989-440086		19891122		
	US 1990-569279		19900821		
	US 1990-569779		19900821		
	US 1991-737883		19910725		
	US 1992-981137		19921124		

OS CASREACT 110:95022; MARPAT 110:95022

GI



AB Title compds. I (R = H, halo; Q = Q1, Q2, Q3; R1 = H, alkyl, OH, halo, NH2, acylamino; R2 = H, alkyl, OH, NH2, alkylsulfonylamino; R3 = H, alkyl, OH; R4 = H, alkylsulfonyl; when R1 = OH, R = R2 = R3 .noteq. H; when R = H, Q .noteq. Q1), useful as nephrovascular tract dilators (no data), are prepd. A soln. of a phenylethanolamine II (prepn. given) in CF3CO2H was treated with concd. H2SO4 in an ice bath to give 6-methoxy-4-(3,4-dimethoxyphenyl)-1,2,3,4-tetrahydroisoquinoline, which was refluxed with 48% HBr to afford I (Q = Q2, R = R1 = R2 = H, R3 = OH).HBr. A capsules contg. I (Q = Q2; R = R3 = H; R1 = R2 = OH) 100, cryst. lactose 200, and Mg stearate 2 mg was given. I at 0.3-100 .mu.g in renal artery of dogs showed max. .apprx.35% increase of a blood flow rate at the highest dose.

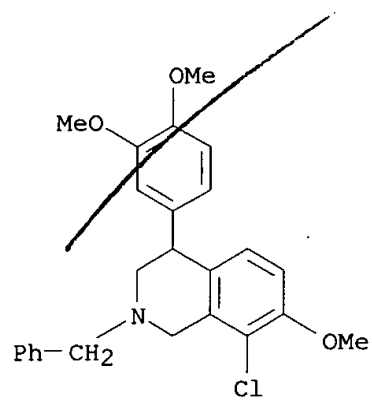
IT **119085-55-1P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and reaction of, in prepn. of isoquinoline, thienopyridine, or thiazolopyridine nephrovascular dilator)

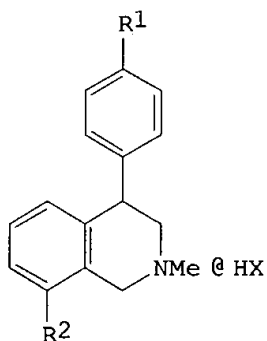
RN 119085-55-1 CAPLUS

CN Isoquinoline, 8-chloro-4-(3,4-dimethoxyphenyl)-1,2,3,4-tetrahydro-7-methoxy-2-(phenylmethyl)- (9CI) (CA INDEX NAME)

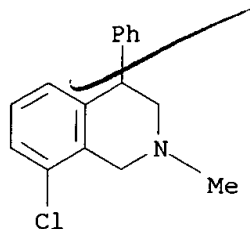


~~148~~ ANSWER 52 OF 100 CAPLUS COPYRIGHT 2003 ACS  
~~AN~~ 1989:57529 CAPLUS  
~~DN~~ 110:57529  
 TI 4-Phenyl-1,2,3,4-tetrahydroisoquinoline derivatives as antiulcer agents  
 and their preparation  
 PA "Farmakhim" State Enterprises, Sofia, Bulg.  
 SO Jpn. Kokai Tokkyo Koho, 9 pp.  
 CODEN: JKXXAF  
 DT **Patent**  
 LA Japanese  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 63126823	A2	19880530	JP 1987-268012	19871023
	HU 44928	A2	19880530	HU 1987-4727	19871021
	HU 203474	B	19910828		
	DD 284788	A7	19901128	DD 1987-308194	19871022
	DK 8705565	A	19880424	DK 1987-5565	19871023
	FI 8704677	A	19880424	FI 1987-4677	19871023
	AU 8780119	A1	19880428	AU 1987-80119	19871023
	AU 612989	B2	19910725		
	CA 1309349	A1	19921027	CA 1987-550075	19871023
PRAI	BG 1986-76843		19861023		
OS	MARPAT 110:57529				
GI					



AB The title compds. I (R1 = H, halo; R2 = halo, amino, ethoxycarbonylamino; X = halo, HO2CCH:CHCO2H), useful as antiulcer agents, were prepd. N-Alkylation of 2-ClC6H4CH2NHMe with C6H5COCH2Br, followed by redn. of the resulting ketone and cyclization, gave 2-methyl-4-phenyl-8-chloro-1,2,3,4-tetrahydroisoquinoline (II). At 1 mg/kg orally, II inhibited stress-induced ulcer in rat by 36.6%.  
 IT **118411-63-5P**  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (prepn. and reaction of, in prepn. of antiulcer agent)  
 RN 118411-63-5 CAPLUS  
 CN Isoquinoline, 8-chloro-1,2,3,4-tetrahydro-2-methyl-4-phenyl- (9CI) (CA INDEX NAME)

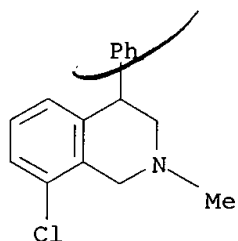


IT 118411-62-4P 118411-63-5P 118411-64-6P  
118411-65-7P 118411-66-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of, as antiulcer agent)

RN 118411-62-4 CAPLUS

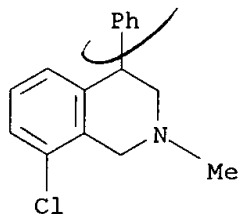
CN Isoquinoline, 8-chloro-1,2,3,4-tetrahydro-2-methyl-4-phenyl-,  
hydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 118411-63-5 CAPLUS

CN Isoquinoline, 8-chloro-1,2,3,4-tetrahydro-2-methyl-4-phenyl- (9CI) (CA INDEX NAME)



RN 118411-64-6 CAPLUS

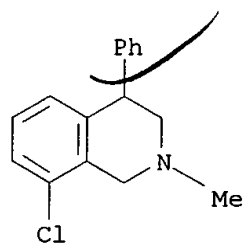
CN Isoquinoline, 8-chloro-1,2,3,4-tetrahydro-2-methyl-4-phenyl-,  
(2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 118411-63-5

09/704,306

CMF C16 H16 Cl N

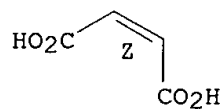


CM 2

CRN 110-16-7

CMF C4 H4 O4

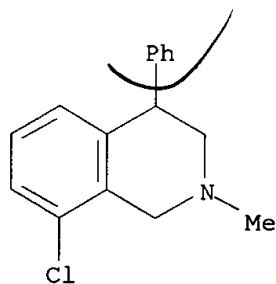
Double bond geometry as shown.



RN 118411-65-7 CAPLUS

CN Isoquinoline, 8-chloro-1,2,3,4-tetrahydro-2-methyl-4-phenyl-,  
hydrochloride, (-)- (9CI) (CA INDEX NAME)

Rotation (-).



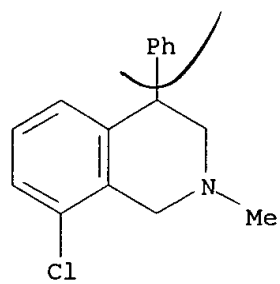
● HCl

RN 118411-66-8 CAPLUS

CN Isoquinoline, 8-chloro-1,2,3,4-tetrahydro-2-methyl-4-phenyl-,  
hydrochloride, (+)- (9CI) (CA INDEX NAME)

Rotation (+).

09/704,306

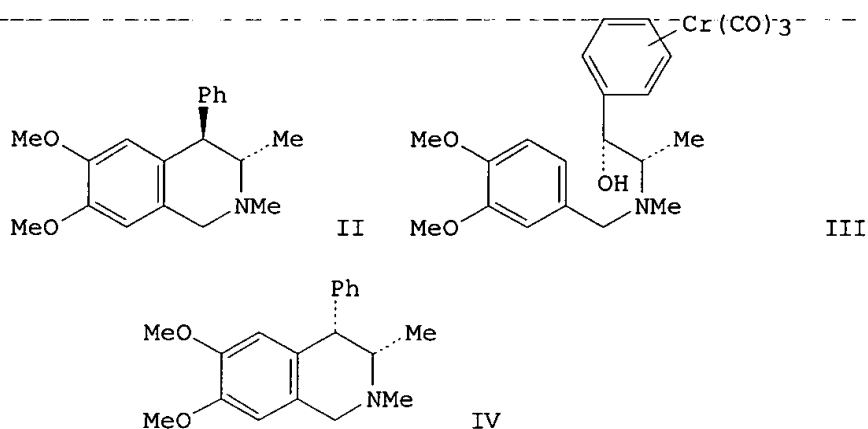


● HCl

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09/704,306

~~148~~ ANSWER 53 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1989:38852 CAPLUS  
DN 110:38852  
TI Complementary stereoselective cyclizations of N-(3,4-dimethoxybenzyl)ephedrine and its chromium tricarbonyl complex to trans- and cis-2,3-dimethyl-4-phenyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolines respectively  
AU Coote, Steven J.; Davies, Stephen G.  
CS Dyson Perrins Lab., Oxford, OX1 3QY, UK  
SO Journal of the Chemical Society, Chemical Communications (1988), (10), 648-9  
CODEN: JCCCAT; ISSN: 0022-4936  
DT Journal  
LA English  
OS CASREACT 110:38852  
GI



AB Treatment of (-)-3,4-(MeO)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CH<sub>2</sub>NMeCHMeCHPhOH (I) with a 1:1 mixt. of CF<sub>3</sub>CO<sub>2</sub>H-H<sub>2</sub>SO<sub>4</sub> at reflux gave 74% (-)-trans-dimethylphenyltetrahydroisoquinoline II stereoselectively with complete inversion of configuration. However, acid treatment of III, the Cr(CO)<sub>3</sub> complex of I, gave only (+)-cis-dimethylphenyltetrahydroisoquinoline IV with complete retention of configuration (double inversion) at the benzylic position.

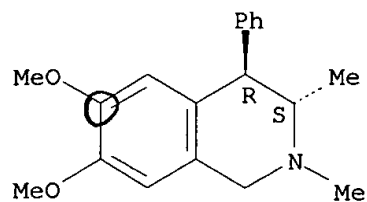
IT 118331-13-8P 118331-15-0P 118331-16-1P 118331-17-2P  
RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)

RN 118331-13-8 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-6,7-dimethoxy-2,3-dimethyl-4-phenyl-, (3S-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

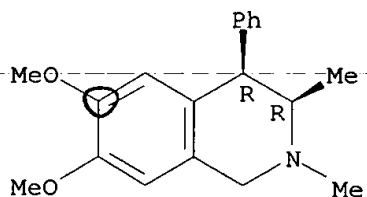




RN 118331-15-0 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-6,7-dimethoxy-2,3-dimethyl-4-phenyl-,  
(3R-cis)- (9CI) (CA INDEX NAME)

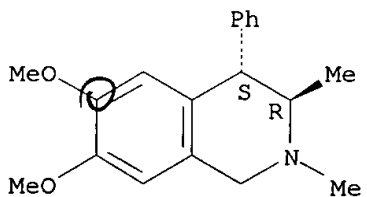
Absolute stereochemistry.



RN 118331-16-1 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-6,7-dimethoxy-2,3-dimethyl-4-phenyl-,  
(3R-trans)- (9CI) (CA INDEX NAME)

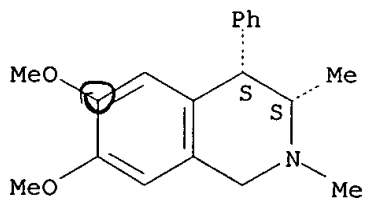
Absolute stereochemistry.



RN 118331-17-2 CAPLUS

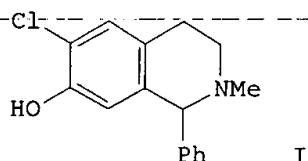
CN Isoquinoline, 1,2,3,4-tetrahydro-6,7-dimethoxy-2,3-dimethyl-4-phenyl-,  
(3S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



09/704,306

~~DI~~ 8 ANSWER 54 OF 100 CAPLUS COPYRIGHT 2003 ACS  
~~AN~~ 1988:528804 CAPLUS  
DN 109:128804  
TI Synthesis and pharmacological characterization of 1-phenyl-, 4-phenyl-,  
and 1-benzyl-1,2,3,4-tetrahydroisoquinolines as dopamine receptor ligands  
AU Charifson, Paul S.; Wyrick, Steven D.; Hoffman, Andrew J.; Simmons, Rosa  
M. Ademe; Bowen, J. Phillip; McDougald, Darryl L.; Mailman, Richard B.  
CS Sch. Pharm., Univ. North Carolina, Chapel Hill, NC, 27599-7360, USA  
SO Journal of Medicinal Chemistry (1988), 31(10), 1941-6  
CODEN: JMCMAR; ISSN: 0022-2623  
DT Journal  
LA English  
OS CASREACT 109:128804  
GI

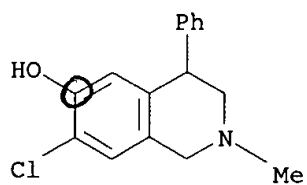


AB A series of 1-phenyl-, 4-phenyl-, and 1-benzyl-1,2,3,4-tetrahydroisoquinolines, e.g., I, were prepd. as ring-contracted analogs of the prototypical D1 dopamine receptor antagonist SCH23390 [(R-(+)-7-chloro-8-hydroxy-3-methyl-1-phenyl-2,3,4,5-tetrahydro-1H-3-benzazepine] starting from 4-MeOC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>CN in 8 steps. The affinity and selectivity of these isoquinolines for D1 receptors were detd. by three biochem. endpoints in membrane homogenates prepd. from rat corpus striatum: the potency to compete for [3H]SCH23390 binding sites; the potency to compete for [3H]spiperone (a D2 receptor ligand) binding sites; and effects on dopamine-stimulated adenylate cyclase. Competitive binding measurements at D1 sites showed SCH23390 to possess the highest affinity, followed by 1-Ph > 1-benzyl > 4-Ph for the isoquinolines. These results were highly correlated with the ability of the test compds. to antagonize dopamine-stimulated adenylate cyclase (r = 0.98). None of the compds. alone stimulated cAMP formation at concns. of 10 nM to 100 .mu.M. D2 competition binding showed the 1-benzyl deriv. to possess the highest affinity, followed by 4-Ph > SCH23390 > 1-Ph. The tertiary 1-Ph deriv. was more potent than the secondary 1-Ph analog in all assays. Interestingly, resoln. and single-crystal x-ray anal. of the tertiary N-methyl-1-phenyltetrahydroisoquinoline showed the most active enantiomer to possess the S abs. configuration, in contrast to the benzazepine (R)-SCH23390.

IT **115514-82-4P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and D1 and D2 dopamine receptor binding and adenylate cyclase inhibition of)

RN 115514-82-4 CAPLUS  
CN 6-Isoquinolinol, 7-chloro-1,2,3,4-tetrahydro-2-methyl-4-phenyl- (9CI) (CA INDEX NAME)

09/704,306

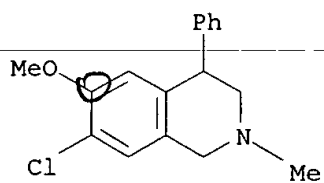


IT 115514-81-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(prepn. and O-demethylation of)

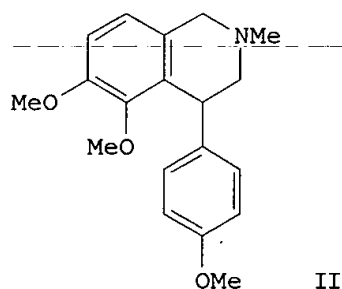
RN 115514-81-3 CAPLUS

CN Isoquinoline, 7-chloro-1,2,3,4-tetrahydro-6-methoxy-2-methyl-4-phenyl-  
(9CI) (CA INDEX NAME)



09/704,306

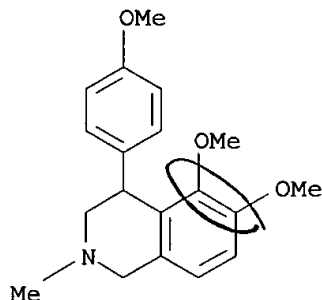
~~148~~ ANSWER 55 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1988:493386 CAPLUS  
DN 109:93386  
TI Efficient synthesis of (.+-.)-latifine dimethyl ether  
AU Gore, Vinayak G.; Narashimhan, Nurani S.  
CS Garware Res. Cent., Univ. Poona, Pune, 411 007, India  
SO Journal of the Chemical Society, Perkin Transactions 1: Organic and  
Bio-Organic Chemistry (1972-1999) (1988), (3), 481-3  
CODEN: JCPRB4; ISSN: 0300-922X  
DT Journal  
LA English  
OS CASREACT 109:93386  
GI



AB 4,5-Dimethoxy-3-(4-methoxyphenyl)phthalide was hydrogenolyzed to give 3,4-dimethoxy-2-(4-methoxybenzyl)benzoic acid (I). The N-methylamide of I was lithiated and treated with DMF to furnish 3,4-dihydro-3-hydroxy-5,6-dimethoxy-4-(4-methoxyphenyl)-2-methylisoquinolin-1(2H)-one, which was reduced with LiAlH<sub>4</sub> to give (.+-.)-latifine di-Me ether (II).

IT **115888-85-2P**, (.+-.)-Latifine dimethyl ether  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 115888-85-2 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-5,6-dimethoxy-4-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



09/704,306

L48 ANSWER 56 OF 100 CAPLUS COPYRIGHT 2003 ACS

AN 1988:221683 CAPLUS

DN 108:221683

TI Diastereomeric complex formation between a novel optically active host and naproxen in aqueous solution

AU Dharanipragada, Ramalinga; Diederich, Francois

CS Dep. Chem. Biochem., Univ. California, Los Angeles, CA, 90024, USA

SO Tetrahedron Letters (1987), 28(22), 2443-6

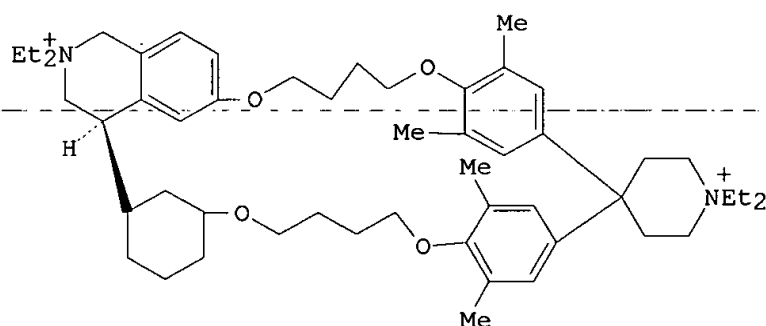
CODEN: TELEAY; ISSN: 0040-4039

DT Journal

LA English

OS CASREACT 108:221683

GI



AB The synthesis of the novel optically active macrocyclic host (+)-I incorporating an unnatural isoquinoline alkaloid as chiral building block is described. The formation of diastereomeric complexes between host (+)-I and (R) and (S)-naproxen in aq. soln. is obsd. by 1H NMR spectroscopy.

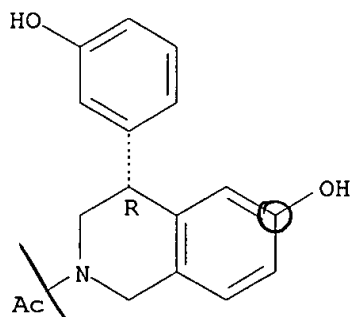
IT 112896-00-1P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and condensation of, with dichlorobutane)

RN 112896-00-1 CAPLUS

CN 6-Isoquinolinol, 2-acetyl-1,2,3,4-tetrahydro-4-(3-hydroxyphenyl)-, (R)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 112896-01-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

09/704,306

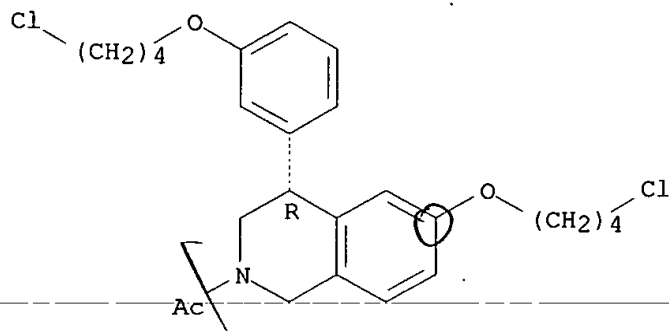
(Reactant or reagent)

(prepn. and cyclocondensation of, with phenol deriv., macrocycle from)

RN 112896-01-2 CAPLUS

CN Isoquinoline, 2-acetyl-6-(4-chlorobutoxy)-4-[3-(4-chlorobutoxy)phenyl]-  
1,2,3,4-tetrahydro-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 112895-99-5P

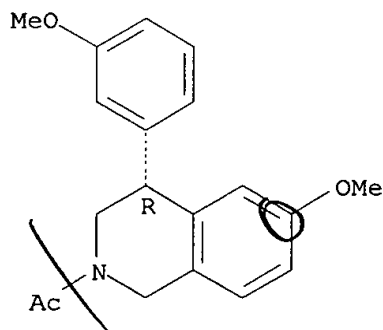
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)

(prepn. and hydrolysis of, phenol deriv. from)

RN 112895-99-5 CAPLUS

CN Isoquinoline, 2-acetyl-1,2,3,4-tetrahydro-6-methoxy-4-(3-methoxyphenyl)-,  
(R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L48 ANSWER 57 OF 100 CAPLUS COPYRIGHT 2003 ACS

AN 1988:216803 CAPLUS

DN 108:216803

TI Pure uptake blockers of dopamine can reduce prolactin secretion: studies with diclofensine

AU Di Renzo, Gianfranco; Amoroso, Salvatore; Taglialatela, Maurizio; Canzoniero, Lorella M. T.; Maida, Paola; Lombardi, Gaetano; Annunziato, Lucio

CS 2nd Sch. Med., Univ. Naples, Naples, 80131, Italy

SO Life Sciences (1988), 42(21), 2161-9

CODEN: LIFSAK; ISSN: 0024-3205

DT Journal

LA English

AB The effects of diclofensine, a pure dopamine (DA) uptake inhibitor on [3H]DA uptake in rat arcuate-periventricular nucleus-median eminence synaptosomes, basal and K+-evoked endogenous DA release from tuberoinfundibular dopaminergic (TIDA) neurons, and the in vivo prolactin (PRL) secretion were studied. Diclofensine (0.01, 0.1, and 1 .mu.M) caused a marked decrease of [3H]DA uptake. In addn., it was unable to stimulate basal endogenous DA release which, on the contrary, was elicited by d-amphetamine in the same concn. (50 .mu.M). On the other hand, diclofensine (50 .mu.M) caused a 3-fold enhancement of K+-evoked DA release. When administered in vivo to male rats, diclofensine reduced basal serum PRL levels. Apparently, the pharmacol. blockade of DA uptake in TIDA neurons is a condition sufficient to cause a redn. of PRL release.

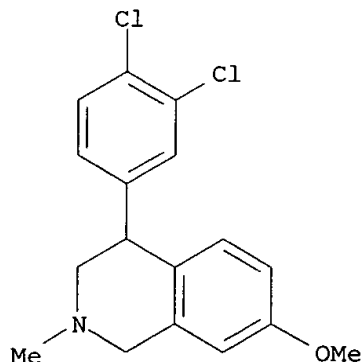
IT 67165-56-4, Diclofensine

RL: BIOL (Biological study)

(prolactin secretion suppression by, brain dopamine uptake inhibition in relation to)

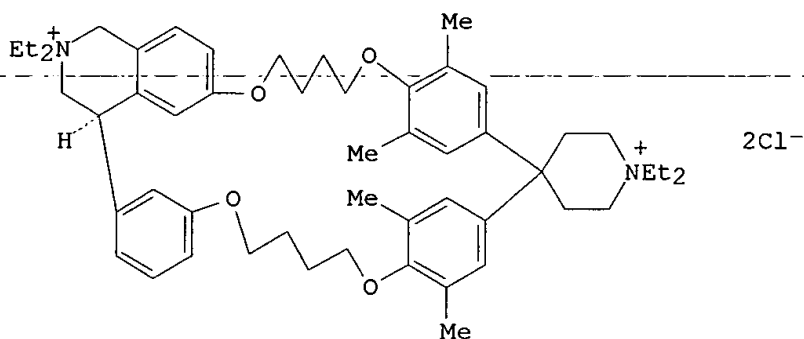
RN 67165-56-4 CAPLUS

CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-(9CI) (CA INDEX NAME)



09/704,306

~~L48~~ ANSWER 58 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1988:130773 CAPLUS  
DN 108:130773  
TI A novel optically active host: design, computer graphics, synthesis, and  
diastereomeric complex formation in aqueous solution  
AU Dharanipragada, Ramalinga; Ferguson, Stephen B.; Diederich, Francois  
CS Dep. Chem. Biochem., Univ. California at Los Angeles, Los Angeles, CA,  
90024, USA  
SO Journal of the American Chemical Society (1988), 110(6), 1679-90  
CODEN: JACSAT; ISSN: 0002-7863  
DT Journal  
LA English  
OS CASREACT 108:130773  
GI



AB The application of mol. mechanics (MM2) to the design of the novel optically active macrocyclic host (+)-I is described. For the synthesis of (+)-I, the unnatural alkaloid 6-methoxy-4-(3-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline was prepd. in 10 steps from m-anisaldehyde and resolved through fractional crystn. of the diastereomeric salts formed with (+)-dibenzoyl-D-tartaric acid. <sup>1</sup>H NMR host-guest complexation anal. in methanolic aq. soln. revealed that (+)-I forms complexes with arom. guests. A high specificity for 2,6-disubstituted naphthalene derivs. was demonstrated. Host (+)-I forms diastereomeric complexes with (R,S)-naproxen and with the Me esters of naproxen (R,S). The observation that the complexes of the Me esters are more stable than the complexes of naproxen leads to the conclusion that ion pairing between the carboxylate of the guest and the quaternary tetrahydroisoquinolinium nitrogen of the host is not effective as a binding and discriminating interaction in the diastereomeric complexes of (R,S)-naproxen. Mol. mechanics in combination with computer graphics (HYDRA) are applied to the anal. of the geometries of free host and of host-guest complexes.

IT 112896-09-0

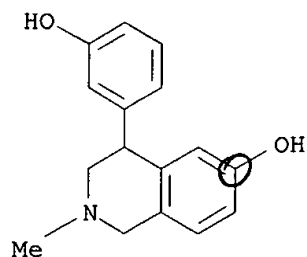
RL: PRP (Properties)

(min. energy conformation of, mol. mechanics calcn. of)

RN 112896-09-0 CAPLUS

CN 6-Isoquinolinol, 1,2,3,4-tetrahydro-4-(3-hydroxyphenyl)-2-methyl- (9CI)  
(CA INDEX NAME)





IT 112896-01-2P

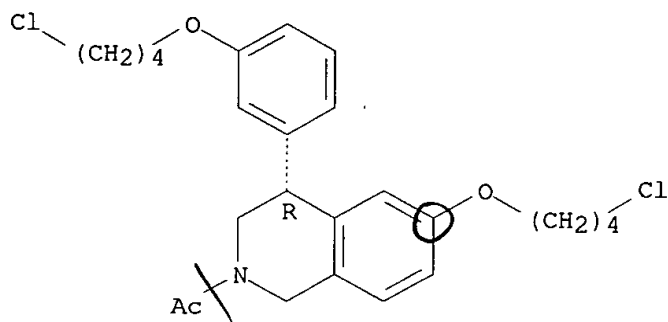
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and cyclization of, with acetylbis(hydroxydimethylphenyl)piperidine)

RN 112896-01-2 CAPLUS

CN Isoquinoline, 2-acetyl-6-(4-chlorobutoxy)-4-[3-(4-chlorobutoxy)phenyl]-1,2,3,4-tetrahydro-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 112895-99-5P

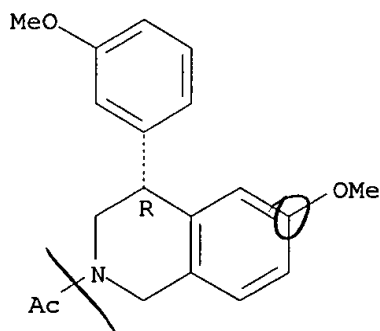
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and demethylation of, with boron tribromide)

RN 112895-99-5 CAPLUS

CN Isoquinoline, 2-acetyl-1,2,3,4-tetrahydro-6-methoxy-4-(3-methoxyphenyl)-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



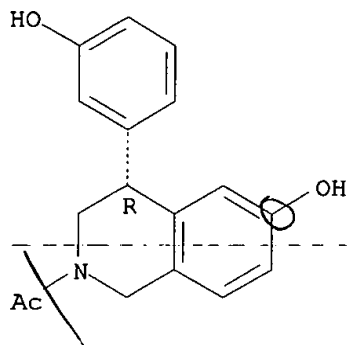
IT **112896-00-1P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and dialkylation of, with dichlorobutane)

RN 112896-00-1 CAPLUS

CN 6-Isoquinolinol, 2-acetyl-1,2,3,4-tetrahydro-4-(3-hydroxyphenyl)-, (R)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

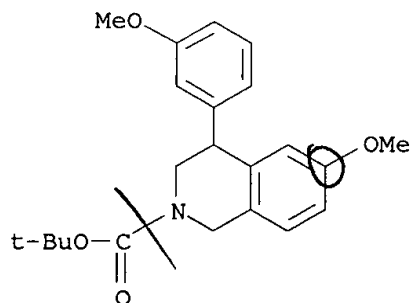


IT **112895-97-3P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and removal of protecting group in, with trifluoroacetic acid)

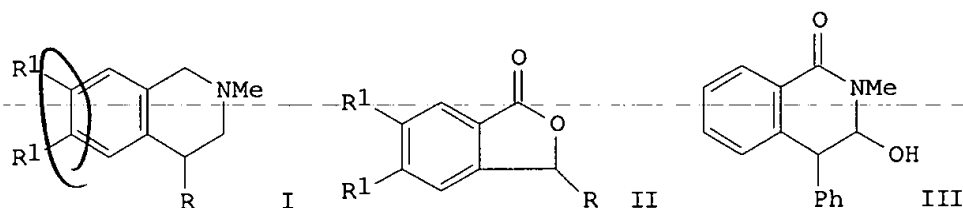
RN 112895-97-3 CAPLUS

CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-6-methoxy-4-(3-methoxyphenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



09/704,306

~~148~~ ANSWER 59 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN- 1987:575850 CAPLUS  
DN 107:175850  
TI An efficient synthesis of 4-aryl-1,2,3,4-tetrahydroisoquinolines  
AU Narasimhan, Nurani S.; Patil, Prakash A.  
CS Garware Res. Cent., Univ. Poona, Pune, 411 007, India  
SO Journal of the Chemical Society, Chemical Communications (1987), (3),  
191-2  
CODEN: JCCCAT; ISSN: 0022-4936  
DT Journal  
LA English  
OS CASREACT 107:175850  
GI



AB Dopamine receptor agonist I (R = Ph, R1 = H) (no data) and the phenolic isoquinoline alkaloid cherylline (I; R = 4-MeOC6H4, R1 = MeO) were prepd. from 3-arylphthalides II (R = Ph, R1 = H; R = 4-MeOC6H4, R1 = MeO) resp. Thus, hydrogenolysis of II (R = Ph, R1 = H) gave o-PhCH2C6H4CO2H which was treated with SOCl2 followed by MeNH2 to give o-PhCH2C6H4CONHMe. Lithiation of the benzamide followed by cyclocondensation with DMF gave tetrahydroisoquinolone III. Dehydration and redn. of III gave I (R = Ph, R1 = H).

IT **110841-21-9P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 110841-21-9 CAPLUS

09/704,306

~~LA~~ 8 ANSWER 60 OF 100 CAPLUS COPYRIGHT 2003 ACS

~~AN~~ 1987:439388 CAPLUS

DN 107:39388

TI Optically active sulfoxide

IN Takano, Seiichi; Ogasawara, Kuniro; Akiyama, Masaji

PA Kawaken Fine Chemicals Co., Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 3 pp.

CODEN: JKXXAF

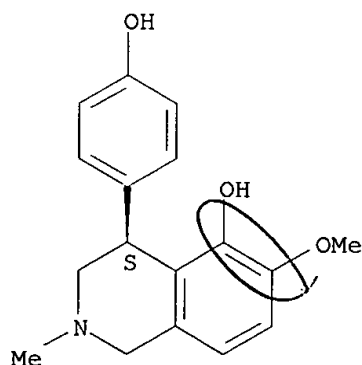
DT **Patent**

LA Japanese

FAN.CNT.1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 62004261	A2	19870110	JP 1985-142285	19850628
PRAI	JP 1985-142285		19850628		
AB	Optically active PhSO <sub>n</sub> CH <sub>2</sub> CH(OH)CH <sub>2</sub> OCH <sub>2</sub> Ph (I; n = 1) (II), useful as intermediate for latifine, pharmaceuticals, and org. reagents, is prepd. (S)-I (n = 0), prepd. by reaction of PhSH with (S)-O-benzylglycidol, was treated with 20% aq. H <sub>2</sub> O <sub>2</sub> at room temp. to give quant. (S)-II.				
IT	<b>93915-33-4</b> , Latifine RL: RCT (Reactant); RACT (Reactant or reagent) (intermediate for, optically active hydroxypropyl Ph sulfoxide deriv. as)				
RN	93915-33-4 CAPLUS				
CN	5-Isoquinolinol, 1,2,3,4-tetrahydro-4-(4-hydroxyphenyl)-6-methoxy-2-methyl-, (4S)- (9CI) (CA INDEX NAME)				

Absolute stereochemistry.



09/704,306

LA8 ANSWER 61 OF 100 CAPLUS COPYRIGHT 2003 ACS

AN 1987:439364 CAPLUS

DN 107:39364

TI Optically active allyl alcohols

IN Takano, Seiichi; Ogasawara, Kuniro; Akiyama, Masaji

PA Kawaken Fine Chemicals Co., Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 3 pp.

CODEN: JKXXAF

DT **Patent**

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 62004240	A2	19870110	JP 1985-142286	19850628
	JP 05050488	B4	19930729		
PRAI	JP 1985-142286		19850628		

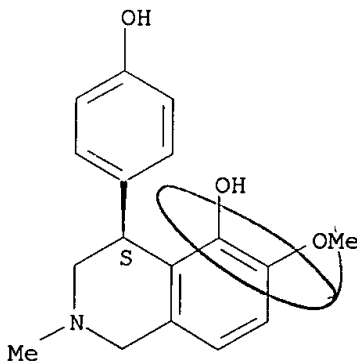
AB Optically active trans-ROC6H4CH:CHCH(OH)CH2OCH2Ph (I; R = alkyl, PhCH2), useful as intermediates for pharmaceuticals, are prepd. BuLi-hexane was added to a soln. of (S)-PhCH2OCH2CH(OH)CH2S(O)Ph and Me2NCH2CH2NMe2 in THF at -55.degree., stirred at room temp. and 4-(PhCH2O)C6H4CH2Cl was added at 0.degree. to give (S)-4-(PhCH2O)C6H4CH2CH[S(O)Ph]CH(OH)CH2OCH2Ph, which was refluxed with CaCO3 in MePh to give 87% (R)-I (R = PhCH2).

IT **93915-33-4**

RL: RCT (Reactant); RACT (Reactant or reagent)  
(intermediates for, optically active allylic alc. deriv. as)

RN 93915-33-4 CAPLUS

CN 5-Isoquinolinol, 1,2,3,4-tetrahydro-4-(4-hydroxyphenyl)-6-methoxy-2-methyl-, (4S)- (9CI) (CA INDEX NAME)



Absolute stereochemistry.

L48 ANSWER 62 OF 100 CAPLUS COPYRIGHT 2003 ACS

AN 1987:433749 CAPLUS

DN 107:33749

TI Biochemical and pharmacological characterization of [3H]GBR 12935 binding in vitro to rat striatal membranes: labeling of the dopamine uptake complex

AU Andersen, Peter H.

CS Dep. Pharmacol., NOVO Ind. A/S, Bagsvaerd, DK-2880, Den.

SO Journal of Neurochemistry (1987), 48(6), 1887-96

CODEN: JONRA9; ISSN: 0022-3042

DT Journal

LA English

AB Binding of the selective dopamine (DA) uptake inhibitor [3H]GBR 12935 to rat striatal membranes was characterized biochem. and pharmacol. [3H]-GBR 12935 binding at 0.degree. was reversible and saturable and Scatchard anal. indicated a single binding site with a dissocn. const. of 5.5 nM and a max. binding capacity of 760 pmol/mg tissue. [3H]GBR 12935 labeled 2 binding sites. One binding site was identified as the classic DA uptake site, since methylphenidate, cocaine, diclofensine, and Lu 19-005 potently inhibited [3H]GBR 12935 binding to it. Binding to the 2nd site was inhibited by high concns. of the above compds. Median inhibitory concn. (IC50) values for inhibition of [3H]GBR 12935 binding to the DA uptake site were proportional to IC50 values for inhibition of DA uptake. However, substrates of DA uptake, e.g., DA and 1-methyl-4-phenylpyridine, and DA releasers, e.g., the amphetamines, inhibited [3H]GBR 12935 binding less than DA uptake. Rate expts. excluded the possibility that these weak inhibitors affected the binding by allosteric coupled binding sites. The 2nd binding site was not a noradrenergic, serotonergic, or GABAergic uptake site. Neither was it a dopaminergic, acetylcholinergic, histaminic, serotonergic, or adrenergic receptor. However, [3H]GBR 12935 was potently displaced from it by disubstituted piperazine derivs., i.e., flupentixol and piflutixol. DA uptake and the DA uptake binding site of [3H]GBR 12935 were located primarily in the striatum, but the piperazine acceptor site was distributed uniformly throughout the brain. Also only the DA uptake binding site was destroyed by 6-hydroxy-DA. Thus, [3H]GBR 12935 labels the classic DA uptake site in rat striatum and also a piperazine acceptor site. Substrates for DA uptake and releasers of DA inhibited [3H]GBR 12935 binding with low potency, but did not alter the rate consts. for [3H]GBR 12935 binding. Therefore inhibitors of DA uptake label the carrier site and prevent the carrier process.

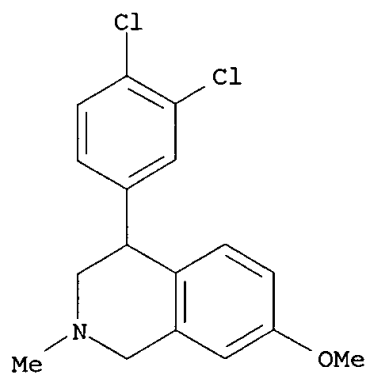
IT 67165-56-4, Diclofensine

RL: BIOL (Biological study)

(dopamine uptake and GBR 12935 binding by striatum inhibition by)

RN 67165-56-4 CAPLUS

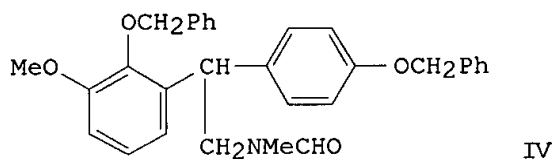
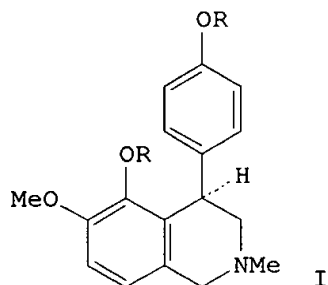
CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-(9CI) (CA INDEX NAME)



09/704,306

L48 ANSWER 63 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AP 1987:176721 CAPLUS  
DN 106:176721  
TI (+)-Latifine  
IN Takano, Seiichi; Ogasawara, Kuniro; Akiyama, Masaji  
PA Kawaken Fine Chemicals Co., Ltd., Japan  
SO Jpn. Kokai Tokkyo Koho, 5 pp.  
CODEN: JKXXAF  
DT Patent  
LA Japanese  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 62004269	A2	19870110	JP 1985-142287	19850628
	JP 06000755	B4	19940105		
PRAI	JP 1985-142287		19850628		
GI					



AB (+)-Latifine (I; R = H) (II) is prepd. by hydrogenolysis of benzyl deriv. (R)-I (R = PhCH<sub>2</sub>) (III). Thus, refluxing a soln. of 0.383 mmol IV and 1.94 mmol POCl<sub>3</sub> in C<sub>6</sub>H<sub>6</sub> gave 76% isoquinoline III, which (0.291 mmol) was hydrogenolyzed in EtOH over 10% Pd-C at 55.degree. to give 100% II. II is useful in pharmaceutical compns.

IT 104372-01-2P

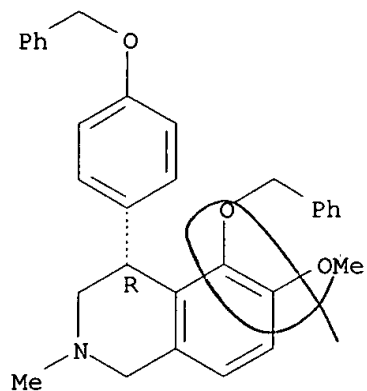
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and hydrogenolysis of)

RN 104372-01-2 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-6-methoxy-2-methyl-5-(phenylmethoxy)-4-[4-(phenylmethoxy)phenyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.





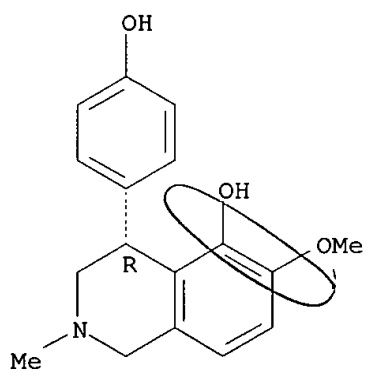
IT **104372-02-3P**, (+)-Latifine

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 104372-02-3 CAPLUS

CN 5-Isoquinolinol, 1,2,3,4-tetrahydro-4-(4-hydroxyphenyl)-6-methoxy-2-methyl-  
, (R)- (9CI) (CA INDEX NAME)

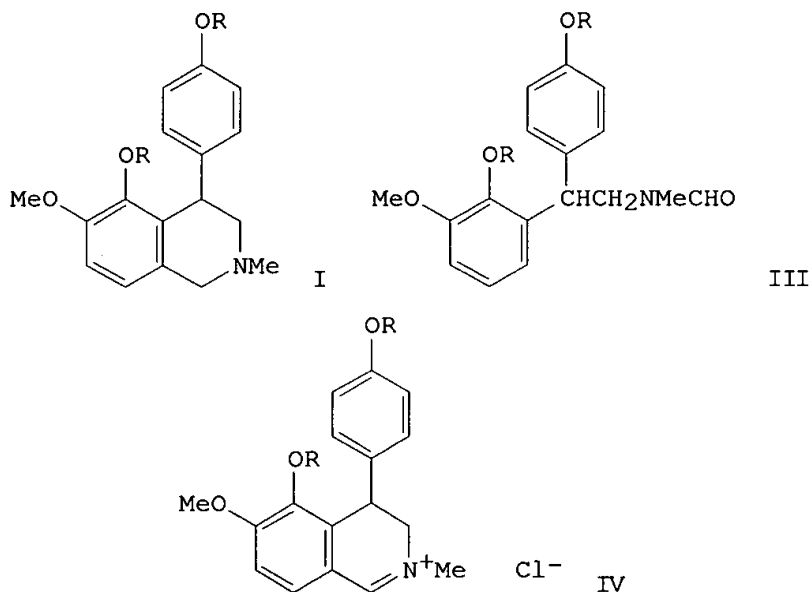
Absolute stereochemistry.



09/704,306

L48 ANSWER 64 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1987:67121 CAPLUS  
DN 106:67121  
TI Latifine  
IN Takano, Seiichi; Ogasawara, Kuniro; Akiyama, Masaji  
PA Kawaken Fine Chemicals Co., Ltd., Japan  
SO Jpn. Kokai Tokkyo Koho, 7 pp.  
CODEN: JKXXAF  
DT Patent  
LA Japanese  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 61183269	A2	19860815	JP 1985-22406	19850207
PRAI	JP 1985-22406		19850207		
OS	CASREACT 106:67121				
GI					

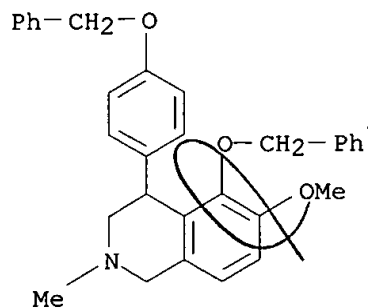


AB (.+-.)-Latifine (I; R = H) (II) is prepd. by thermal cyclization of formamide deriv. III (R = OH-protecting group) and redn. of the resultant isiquinolinium salt IV. Thus, refluxing 0.34 mmol POCl<sub>3</sub> and 0.067 mol III (R = PhCH<sub>2</sub>) in C<sub>6</sub>H<sub>6</sub> gave IV (R = PhCH<sub>2</sub>, X = Cl), which was reduced with 0.67 mmol NaBH<sub>4</sub> in MeOH under cooling at 50.degree. to give 51% I (R = PhCH<sub>2</sub>) (V). Heating a mixt. of 25 mg 10% Pd-C and 94 mg V in EtOH at 55.degree. gave 85% II.

IT **97455-98-6P**  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and redn. of)

RN 97455-98-6 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-6-methoxy-2-methyl-5-(phenylmethoxy)-4-[4-(phenylmethoxy)phenyl]- (9CI) (CA INDEX NAME)

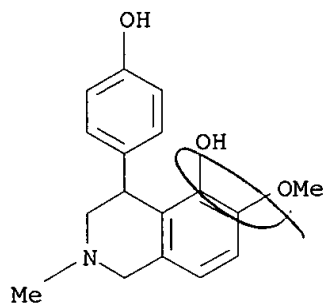


IT **97549-48-9P**, (.-.)Latifine

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

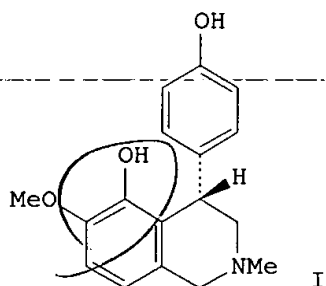
RN 97549-48-9 CAPLUS

CN 5-Isoquinolinol, 1,2,3,4-tetrahydro-4-(4-hydroxyphenyl)-6-methoxy-2-methyl-  
(9CI) (CA INDEX NAME)



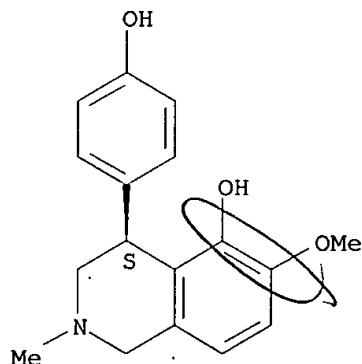
09/704,306

L48 ANSWER 65 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1987:18899 CAPLUS  
DN 106:18899  
TI Structure and synthesis of a novel alkaloid, latifine, from *Crinum latifolium*  
AU Kobayashi, Shigeru; Tokumoto, Toshihiro; Iguchi, Seiichiro; Kihara, Masaru; Imakura, Yasuhiro; Taira, Zenei  
CS Fac. Pharm. Sci., Tokushima Univ., Tokushima, 770, Japan  
SO Journal of Chemical Research, Synopses (1986), (8), 280-1  
CODEN: JRPSDC; ISSN: 0308-2342  
DT Journal  
LA English  
OS CASREACT 106:18899  
GI



AB The structure of the title alkaloid (I), isolated from *C. latifolium* (1984) was detd. by spectral and crystallog. methods. The racemate of I was prepd. in 4 steps from 6-bromoisovanillin and (+-)-4-HOC6H4CH(OH)CH2NH2.HCl.  
IT 93915-33-4P, Latifine  
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (prepn. and crystal and mol. structure of)  
RN 93915-33-4 CAPLUS  
CN 5-Isoquinolinol, 1,2,3,4-tetrahydro-4-(4-hydroxyphenyl)-6-methoxy-2-methyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 93915-34-5P 97549-48-9P

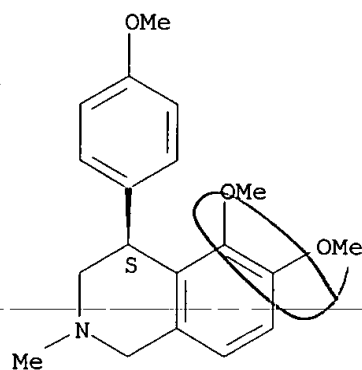
09/704,306

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 93915-34-5 CAPLUS

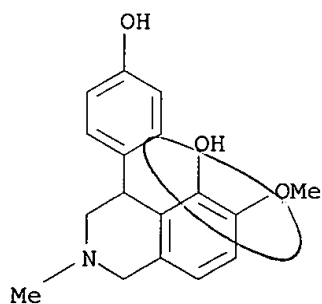
CN Isoquinoline, 1,2,3,4-tetrahydro-5,6-dimethoxy-4-(4-methoxyphenyl)-2-methyl-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 97549-48-9 CAPLUS

CN 5-Isoquinolinol, 1,2,3,4-tetrahydro-4-(4-hydroxyphenyl)-6-methoxy-2-methyl- (9CI) (CA INDEX NAME)

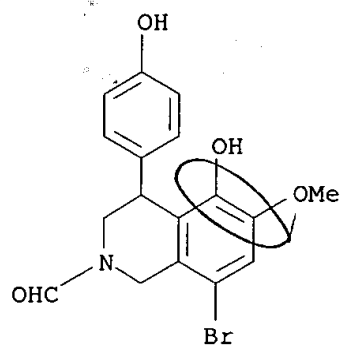


IT 105892-79-3P

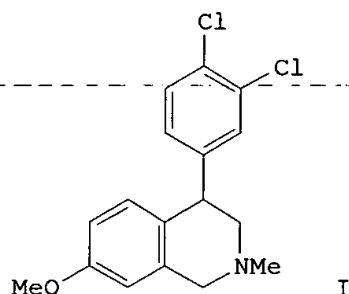
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of, as intermediate in prepn. of latifine racemate)

RN 105892-79-3 CAPLUS

CN 2(1H)-Isoquinolinecarboxaldehyde, 8-bromo-3,4-dihydro-5-hydroxy-4-(4-hydroxyphenyl)-6-methoxy- (9CI) (CA INDEX NAME)



L48 ANSWER 66 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1986:603049 CAPLUS  
DN 105:203049  
TI Preclinical pharmacology of diclofensine  
AU Burkard, W. P.; Bonetti, E. P.; Carruba, M. O.; Da Prada, M.; Keller, H.  
H.; Kettler, R.; Richards, J. G.; Schaffner, R.; Scherschlicht, R.;  
Haefely, W.  
CS Pharma Ferschung, F. Hoffmann-La Roche and Co. A.-G., Basel, 4002, Switz.  
SO Drug Development and Evaluation (1986), 12 (Neue Aspekte Ther.  
Antidepressiva), 71-93  
CODEN: DDEVD6; ISSN: 0343-4842  
DT Journal; General Review  
LA German  
GI

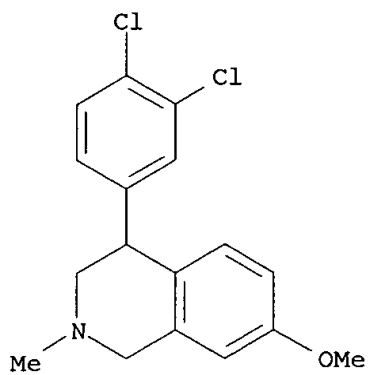


AB Diclofensine (I) [67165-56-4] is an antidepressant which inhibits neuronal uptake of all 3 biogenic monoamines. I is the strongest inhibitor of dopamine [51-61-6] uptake known. In nontoxic doses, I has no amine-liberating action, unlike amphetamine or nomifensine. In contrast to almost all tricyclic antidepressants, I does not block cholinergic receptors. In a variety of pharmacol. studies, no serious side effects of I have been obsd. A review of the literature on I pharmacol. is included.

IT **67165-56-4**  
RL: BIOL (Biological study)  
(monoamine uptake by neuron inhibition by and pharmacol. of)

RN 67165-56-4 CAPLUS

CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-  
(9CI) (CA INDEX NAME)

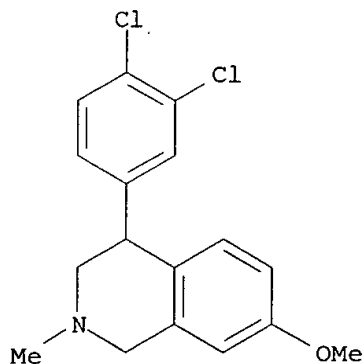




L48 ANSWER 67 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1986:583757 CAPLUS  
DN 105:183757  
TI The toxicology of diclofensine  
AU Schlaeppli, B.  
CS Biol. Pharma Ferschung, F. Hoffmann La Roche and Co. A.-G., Basel, 4002, Switz.  
SO Drug Development and Evaluation (1986), 12 (Neue Aspekte Ther. Antidepressiva), 107-16  
CODEN: DDEV6; ISSN: 0343-4842  
DT Journal  
LA German  
AB In acute toxicity expts. with diclofensine (I) [67165-56-4], no mortality was seen in mice and rats receiving, resp., 250 and 2000 times the therapeutic dose (.apprx.1 mg/kg). In subchronic and chronic studies in dogs (.ltoreq.12 mo) and rats (.ltoreq.18 mo), high plasma levels of I (as compared with human therapeutic levels) were tolerated well. No cardiotoxic or hepatotoxic effects were obsd. I is neither a teratogen, a mutagen, nor a carcinogen. The danger from long-term use appears to be small.

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IT 67165-56-4  
RL: BIOL (Biological study)  
(acute and chronic toxicity of)  
RN 67165-56-4 CAPLUS  
CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl- (9CI) (CA INDEX NAME)



09/704,306

L48 ANSWER 68 OF 100 CAPLUS COPYRIGHT 2003 ACS

AN 1986:583756 CAPLUS

DN 105:183756

TI Effect of declofensine, nomifensine, and d-amphetamine on the cerebral absorption of 2-deoxyglucose as an indicator of glucose turnover in the brain

AU Lorez, H. P.

CS Pharmaferschung, F. Hoffmann La Roche and Co. A.-G., Basel, 4002, Switz.

SO Drug Development and Evaluation (1986), 12 (Neue Aspekte Ther. Antidepressiva), 95-105

CODEN: DDEVD6; ISSN: 0343-4842

DT Journal

LA German

AB The effect of D-amphetamine [51-64-9] (0.18-5.0 mg amphetamine sulfate/kg, i.v.), diclofensine methanesulfonate [104855-34-7], and nomifensine maleate [32795-47-4] (0.55-15 mg/kg, i.v.) on glucose [50-99-7] turnover in the brain was studied by means of radiolabeled 2-deoxy-D-glucose in rats. At low dosages, amphetamine and (less strongly) nomifensine increased tissue label in the diencephalon, substantia nigra, neostriatum, and cerebellum. Diclofensine, however, raised tissue label only slightly, and only in the cerebellum. The increase in glucose turnover induced by amphetamine and nomifensine particularly in brain regions activated by motor activity corresponds to the motor activity-stimulating properties of the 2 drugs. Diclofensine stimulates motor activity much less than do the other 2 drugs.

IT 104855-34-7

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(glucose turnover in brain response to)

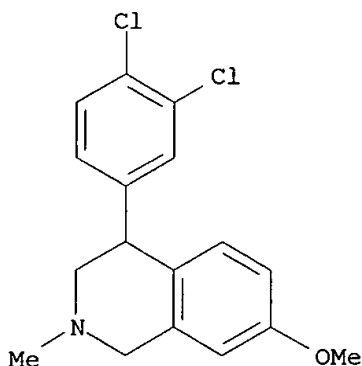
RN 104855-34-7 CAPLUS

CN' Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 67165-56-4

CMF C17 H17 Cl2 N O

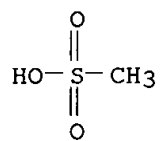


CM 2

CRN 75-75-2

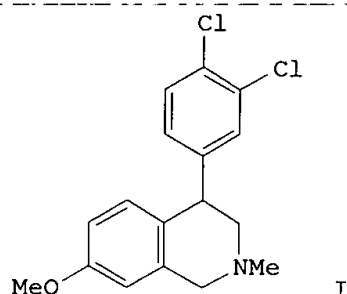
09/704,306

CMF C H4 O3 S



09/704,306

L48 ANSWER 69 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1986:564353 CAPLUS  
DN 105:164353  
TI Quantitative determination of diclofensine (Ro 8-4650) in plasma by  
capillary column gas chromatography, mass spectrometry, and selective ion  
detection  
AU Ranalder, U. B.  
CS Abt. Zent. Ferschung., F. Hoffmann-LaRoche and Co. A.-G., Basel, 4002,  
Switz.  
SO Drug Development and Evaluation (1986), 12(Neue Aspekte Ther.  
Antidepressiva), 117-25  
CODEN: DDEVD6; ISSN: 0343-4842  
DT Journal  
LA German  
GI

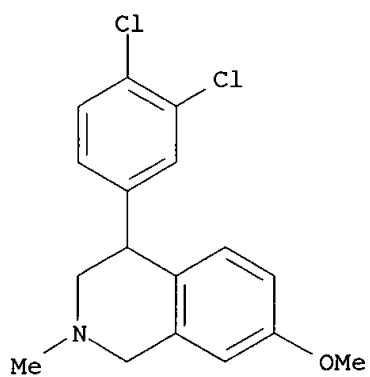


AB Diclofensine (I) [67165-56-4] and its internal std., deuterated  
I (R.delta. 8-4650/027) were extd. from plasma with Et2O, followed by  
back-extn. into 1N H2SO4 and re-extn. into Et2O after alkalization of  
the aq. ext. Gas chromatog. was carried out on polymd. SE 54, followed by  
mass-spectrometric anal. of the fragmentation at m/z 243 (246 for the  
std.). The detection limit was 0.3 mg I/mL plasma, the total extn. yield  
57%, and the reproducibility (in the range 1-10 mg/mL) .+-8.5%.

IT **67165-56-4**  
RL: ANT (Analyte); ANST (Analytical study)  
(detn. of, in blood plasma by gas chromatog.-mass spectrometry)

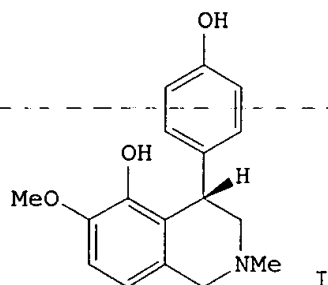
RN 67165-56-4 CAPLUS

CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-  
(9CI) (CA INDEX NAME)



09/704,306

~~L48~~ ANSWER 70 OF 100 CAPLUS COPYRIGHT 2003 ACS  
~~AN~~ 1986:553372 CAPLUS  
DN 105:153372  
TI Total synthesis of (.-.)- and (+)-latifine  
AU Takano, Seiichi; Akiyama, Masashi; Ogasawara, Kunio  
CS Pharm. Inst., Tohoku Univ., Sendai, 980, Japan  
SO Journal of the Chemical Society, Perkin Transactions 1: Organic and  
Bio-Organic Chemistry (1972-1999) (1985), (11), 2447-53  
CODEN: JCPRB4; ISSN: 0300-922X  
DT Journal  
LA English  
OS CASREACT 105:153372  
GI

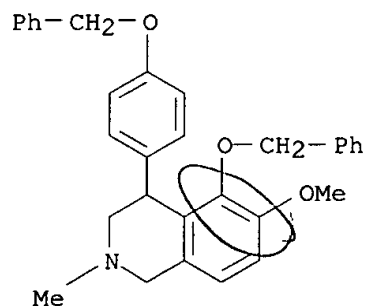


AB Racemic latifine [(.-.)-(I)], a new representative of the rare phenolic Amaryllidaceae alkaloids, was synthesized by employing the Claisen rearrangement of 4-benzyloxycinnamyl 2-methoxyphenyl ether as a key step. Based on the racemic synthesis, (R)-(+)-I, the unnatural enantiomer, was also synthesized from (R)-O-benzylglycidol via (S)-1-benzyloxy-3-phenylthioprop-2-ol as a key intermediate.

IT **97455-98-6P 104372-01-2P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of, in total synthesis of latifine)

RN 97455-98-6 CAPLUS

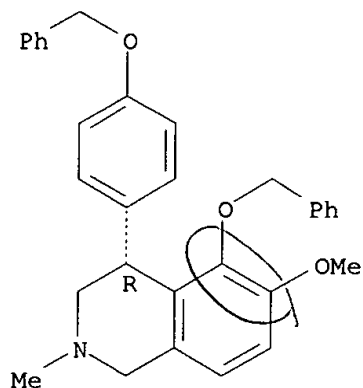
CN Isoquinoline, 1,2,3,4-tetrahydro-6-methoxy-2-methyl-5-(phenylmethoxy)-4-[4-(phenylmethoxy)phenyl]- (9CI) (CA INDEX NAME)



RN 104372-01-2 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-6-methoxy-2-methyl-5-(phenylmethoxy)-4-[4-(phenylmethoxy)phenyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

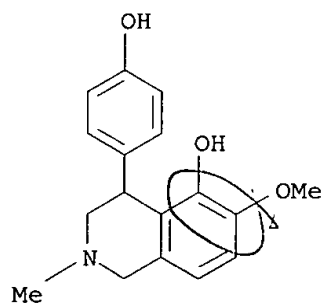


IT 97549-48-9P 104372-02-3P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(total synthesis of)

RN 97549-48-9 CAPLUS

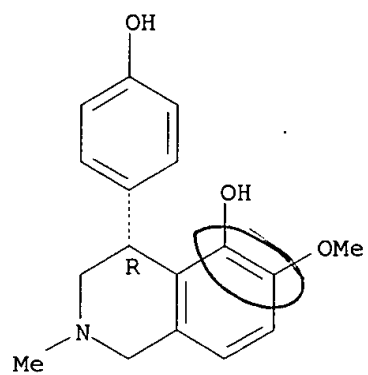
CN 5-Isoquinolinol, 1,2,3,4-tetrahydro-4-(4-hydroxyphenyl)-6-methoxy-2-methyl-  
(9CI) (CA INDEX NAME)



RN 104372-02-3 CAPLUS

CN 5-Isoquinolinol, 1,2,3,4-tetrahydro-4-(4-hydroxyphenyl)-6-methoxy-2-methyl-  
, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.





L48 ANSWER 71 OF 100 CAPLUS COPYRIGHT 2003 ACS

AN 1986:527404 CAPLUS

DN 105:127404

TI Antidepressant competition for adenosine binding sites and chronic doxepin induced increases in adenosine receptors

AU Lewis, J. L.; Geiger, J. D.

CS Fac. Med., Univ. Manitoba, Winnipeg, MB, R3E 0W3, Can.

SO Proceedings of the Western Pharmacology Society (1986), 29, 265-9

CODEN: PWPSA8; ISSN: 0083-8969

DT Journal

LA English

AB Antidepressants interacted competitively with putative adenosine transport sites and adenosine receptors of rat brain membranes in a study of the abilities of 12 antidepressants to compete with 3H-labeled nitrobenzylthioinosine [38048-32-7] binding to putative adenosine transport sites and with 3H-labeled cyclohexyladenosine (II) [36396-99-3] binding to adenosine receptors. Chronic treatment of rats with doxepin [1668-19-5] increased the no. of adenosine receptors (as detd. by II binding to receptor sites of the brain). Brain adenosine deaminase [9026-93-1] was not affected by 5 of the antidepressants (clorgyline [17780-72-2], amitriptyline [50-48-6], zimelidine [56775-88-3], and doxepin).

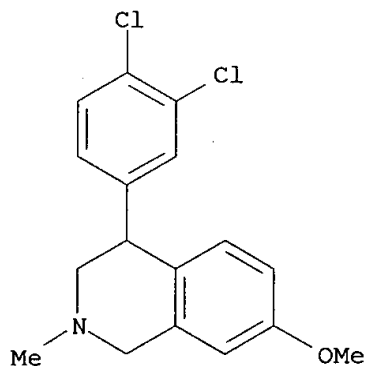
IT 67165-56-4

RL: PRP (Properties)

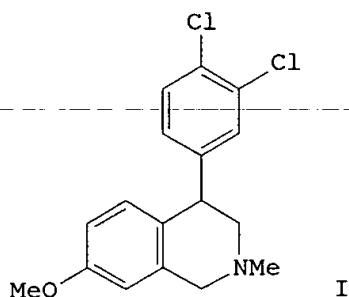
(interaction of, with cyclohexyladenosine binding to adenosine receptors and nitrobenzylthioinosine binding to putative adenosine transport sites, of brain)

RN 67165-56-4 CAPLUS

CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl- (9CI) (CA INDEX NAME)



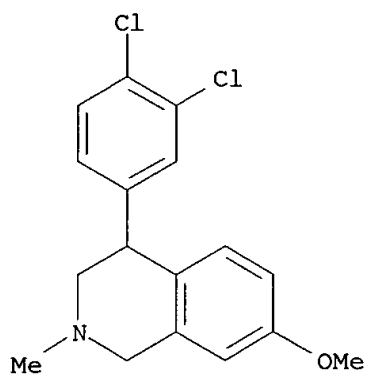
L48 ANSWER 72 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1986:435449 CAPLUS  
DN 105:35449  
TI Effect of diclofensine, a novel antidepressant, on peripheral adrenergic function  
AU Gasic, S.; Korn, A.; Eichler, H. G.  
CS Dep. Clin. Pharmacol., I. Med. Univ., Vienna, A-1090, Austria  
SO Clinical Pharmacology & Therapeutics (St. Louis, MO, United States) (1986), 39(5), 582-5  
CODEN: CLPTAT; ISSN: 0009-9236  
DT Journal  
LA English  
GI



AB The action of Ro 8-4650 (diclofensine) (I) [67165-56-4] on peripheral neuronal adrenergic function was studied in normal subjects through tests of the blood pressure response to norepinephrine (NE) [51-41-2], tyramine [51-67-2], phenylephrine (PE) [59-42-7]. The blood pressure response to NE was enhanced and that to tyramine was decreased by diclofensine, as a result of its inhibitive action on peripheral neuronal amine uptake. PE sensitivity was also enhanced by diclofensine as well as after a single dose of desmethylinipramine (DMI) [50-47-5]. In contrast to the common opinion that PE does not interact with the neuronal uptake mechanism, the increase in PE-induced blood pressure response after diclofensine and DMI suggests that PE, a nonbiogenic amine, does indeed enter into the peripheral adrenergic neuron. This neuronal uptake may probably be unmasked only by powerful NE uptake inhibitors such as DMI or diclofensine.

IT **67165-56-4**  
RL: BIOL (Biological study)  
(peripheral adrenergic neurotransmission response to, in humans)

RN 67165-56-4 CAPLUS  
CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl- (9CI) (CA INDEX NAME)



L48 ANSWER 73 OF 100 CAPLUS COPYRIGHT 2003 ACS

AN 1985:482205 CAPLUS

DN 103:82205

TI Sodium dependent [3H]cocaine binding associated with dopamine uptake sites in the rat striatum and human putamen decreases after dopaminergic denervation and in Parkinson's disease

AU Schoemaker, H.; Pimoule, C.; Arbilla, S.; Scatton, B.; Javoy-Agid, F.; Langer, S. Z.

CS Lab. Etud. Rech. Synthelabo, Synthelabo, Paris, F-75013, Fr.

SO Naunyn-Schmiedeberg's Archives of Pharmacology (1985), 329(3), 227-35  
CODEN: NSAPCC; ISSN: 0028-1298

DT Journal

LA English

AB The binding of 3H-labeled cocaine [50-36-2], an inhibitor of dopamine [51-61-6] uptake, to the postmortem human putamen was studied and compared to that in the rat striatum. Satn. anal. of [3H]cocaine binding to the human putamen revealed the presence of a high-affinity component of binding with a disso. const. (Kd) of 0.21 .mu.M and a max. binding capacity (Bmax) of 1.47 pmol/mg protein. In addn., a low-affinity component (Kd = 26.4 .mu.M) was demonstrated, having a Bmax of 42.2 pmol/mg protein. In the rat striatum, [3H]cocaine binding was both of high (Kd = 0.36 .mu.M, Bmax = 5.56 pmol/mg protein) and low affinity (Kd = 25.9 .mu.M, Bmax = 35.6 pmol/mg protein). Pharmacol. characterization of high-affinity [3H]cocaine binding to rat striatal membranes indicated an assocn. with the neuronal dopamine transporter. The doses for 50% inhibition of [3H]cocaine binding (IC50) of 8 selected drugs in the rat striatum were correlated with their potency to inhibit [3H]dopamine uptake into slices of the rat striatum. [3H]cocaine binding was stereospecifically inhibited by (+)-nomifensine [89664-20-0] and (+)-diclofensine [50560-38-8] which were 50-80-fold more active than their resp. (-) isomers. Drugs with dopamine-releasing activity were more potent at inhibiting [3H]dopamine uptake than at competing for the high-affinity site of [3H]cocaine binding. A correlation was found between IC50 values for [3H]cocaine binding in the rat striatum and the human putamen. Further evidence in support of an assocn. of [3H]cocaine binding in the rat striatum with the dopamine transporter was obtained from lesion studies. Thus, intranigral 6-hydroxydopamine administration produced a marked (67%) decrease in striatal [3H]cocaine binding. Also, in the human putamen high-affinity [3H]cocaine binding sites appear localized on dopaminergic nerve terminals, as evidenced by a prominent decrease in binding in the putamen obtained from subjects with Parkinson's disease. [3H]cocaine may thus be a useful ligand to examine the dopamine transporter in the rat striatum and the human putamen. Therefore it offers a new and valuable approach in the study of drug effects and neuropsychiatric diseases.

IT 50560-38-8 50560-45-7

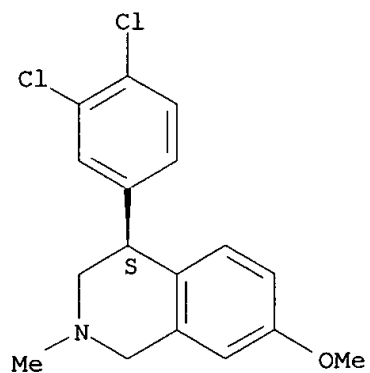
RL: BIOL (Biological study)

(cocaine binding by striatum inhibition by, stereospecificity of)

RN 50560-38-8 CAPLUS

CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-, (4S)- (9CI) (CA INDEX NAME)

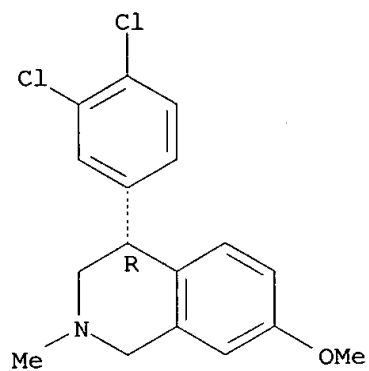
Absolute stereochemistry.



RN 50560-45-7 CAPLUS

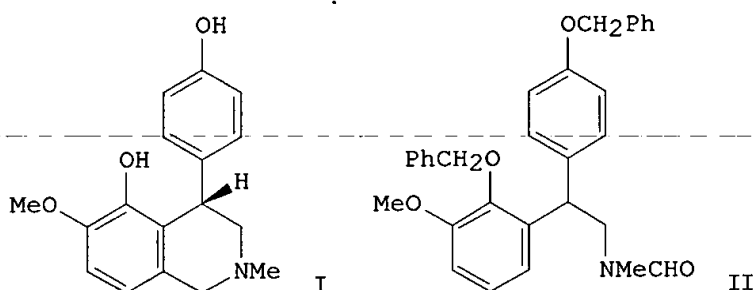
CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-  
 -----, (4R)- (9CI)- (CA INDEX NAME) -----

Absolute stereochemistry.



09/704,306

LA8 ANSWER 74 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1985:471567 CAPLUS  
DN 103:71567  
TI The total synthesis of (+-)-latifine  
AU Takano, Seiichi; Akiyama, Masashi; Ogasawara, Kunio  
CS Pharm. Inst., Tohoku Univ., Sendai, 980, Japan  
SO Chemistry Letters (1985), (4), 505-6  
CODEN: CMLTAG; ISSN: 0366-7022  
DT Journal  
LA English  
OS CASREACT 103:71567  
GI

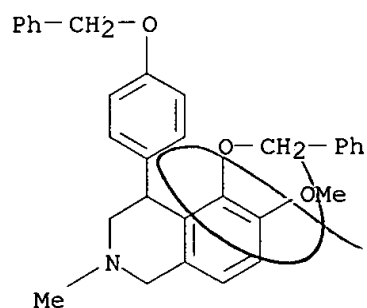


AB Latifine (I), a novel phenolic isoquinoline base from *Crinum latifolium* L. (Amaryllidaceae), was prepd. in 12 steps from p-PhCH<sub>2</sub>OC<sub>6</sub>H<sub>4</sub>CHO via cyclization of the amide II.

IT **97455-98-6P**  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and hydrazinolysis of)

RN 97455-98-6 CAPLUS

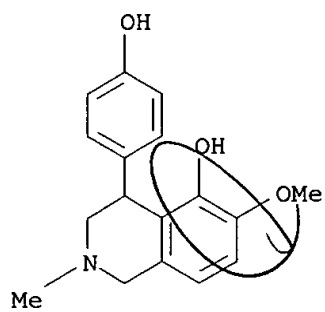
CN Isoquinoline, 1,2,3,4-tetrahydro-6-methoxy-2-methyl-5-(phenylmethoxy)-4-[4-(phenylmethoxy)phenyl]- (9CI) (CA INDEX NAME)



IT **97549-48-9P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 97549-48-9 CAPLUS

CN 5-Isoquinolinol, 1,2,3,4-tetrahydro-4-(4-hydroxyphenyl)-6-methoxy-2-methyl- (9CI) (CA INDEX NAME)



L48 ANSWER 75 OF 100 CAPLUS COPYRIGHT 2003 ACS

AN 1985:464258 CAPLUS

DN 103:64258

TI Determination of diclofensine, an antidepressant agent, and its major metabolites in human plasma by high-performance liquid chromatography with fluorometric detection

AU Strojny, N.; De Silva, J. A. F.

CS Dep. Pharmacokinet., Biopharm. Drug Metab., Hoffmann-La Roche Inc., Nutley, NJ, 07110, USA

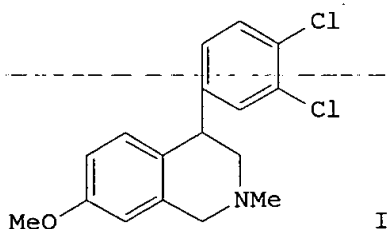
SO Journal of Chromatography (1985), 341(2), 313-31

CODEN: JOCRAM; ISSN: 0021-9673

DT Journal

LA English

GI



AB A sensitive and selective HPLC procedure for the detn. of diclofensine (I) [67165-56-4] and its key metabolites in human plasma is described. The assay involves deproteinization of plasma, overnight glucuronidase incubation to hydrolyze the major metabolite, a glucuronide, extn. of the parent compd. and its deconjugated metabolites from the alkalized aq. phase into Et<sub>2</sub>O-EtOH (95:5), the residue of which is alkylated with 2-iodopropane dissolved in Me<sub>2</sub>CO by the use of solid KOH as a catalyst. The compds. are extd. from the reaction mixt. into Et<sub>2</sub>O, after adding EtOH-H<sub>2</sub>O-AcOH (55:40:5), the residue of which is dissolved in 0.05 M H<sub>2</sub>SO<sub>4</sub> and reacted with mercuric acetate at 100.degree., which oxidizes tertiary tetrahydroisoquinolines to their 3,4-dihydroisoquinoline derivs., followed by a photochem. reaction in the same soln. to form intensely fluorescent isoquinolinium derivs. An aliquot of this reaction mixt. is injected onto a reversed-phase HPLC column (5- $\mu$ m Nova-Pac C18 phase in a radial compression cartridge, 10 cm .times. 8 mm), with the mobile phase [0.25 M triethylammonium phosphate (pH 2.5)- 0.25 M AcOH-MeOH-MeCN-THF (150:350:125:375:25)]. The void vol. (V<sub>0</sub>) is approx. 1.4 min and the retention times of the resp. isoquinolinium derivs. of I are approx. 3.5 min, internal std. approx. 4.2 min, nordiclofensine [97453-62-8] approx. 5 min, while the 2 phenolic metabolites give peaks at 6.4 min and 10.4 min. The derivs. are detected by fluorescence. The method was used to det. plasma concns. of I and its major phenolic metabolite (aglycon) in plasma in 2 normal volunteers following a single oral 45-mg dose and following 7 consecutive days of oral dosing of 45 mg 3 times a day as part of a multiple ascending dose tolerance study.

IT 67165-56-4 97453-63-9

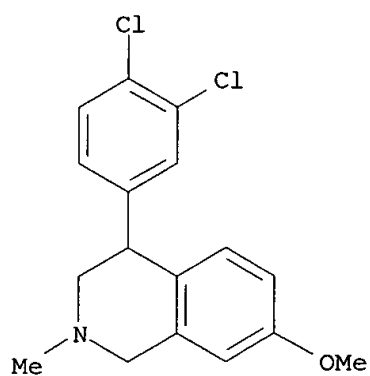
RL: ANT (Analyte); ANST (Analytical study)

(detn. of, in human blood by HPLC with fluorometric detection)

RN 67165-56-4 CAPLUS

CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl- (9CI) (CA INDEX NAME)





RN 97453-63-9 CAPLUS

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L48 ANSWER 76 OF 100 CAPLUS COPYRIGHT 2003 ACS

AN 1985:416755 CAPLUS

DN 103:16755

TI Neurochemical profile of Lu 19-005, a potent inhibitor of uptake of dopamine, noradrenaline, and serotonin

AU Hyttel, John; Larsen, Jens Joergen

CS Dep. Pharmacol. Toxicol., H. Lundbeck A/S, Copenhagen-Valby, Den.

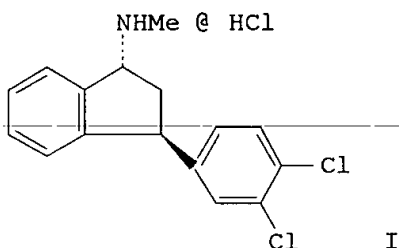
SO Journal of Neurochemistry (1985), 44(5), 1615-22

CODEN: JONRA9; ISSN: 0022-3042

DT Journal

LA English

GI



AB Lu 19-005 (I) [96850-13-4] was a potent inhibitor of the uptake of dopamine (DA) [51-61-6], noradrenaline (NA) [51-41-2], and 5-HT [50-67-9] by rat brain synaptosomes. In this respect it resembled diclofensine [67165-56-4], whereas compds. such as GBR 13.069 [77862-93-2] and bupropion [34911-55-2] were more selective DA-uptake inhibitors. Although I released DA at higher concns. it must be considered as an uptake inhibitor, as the accumulation of DA was inhibited at much lower concns. I attenuated the DA and NA depletion caused by 6-hydroxydopamine in mouse brain. These properties confirm the DA- and NA-uptake-inhibiting properties of the compd. In receptor-binding models and functional in vitro tests, I was devoid of dopaminergic-, serotonergic-, noradrenergic-, histaminic-, or cholinergic-inhibiting properties. Since DA, NA, and 5-HT seem to be involved in depression, the profile of I (with equally potent activity on the 3 neuronal systems) makes it an interesting exptl. tool and a potential new antidepressant agent.

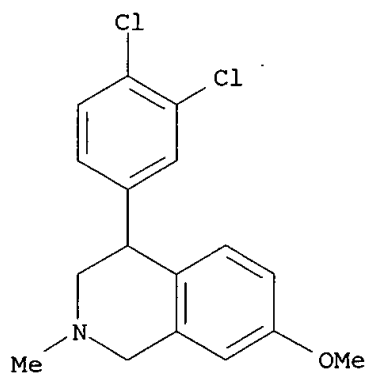
IT **67165-56-4**

RL: BIOL (Biological study)

(neurotransmitter uptake by brain synaptosomes response to, Lu 19-005 in relation to)

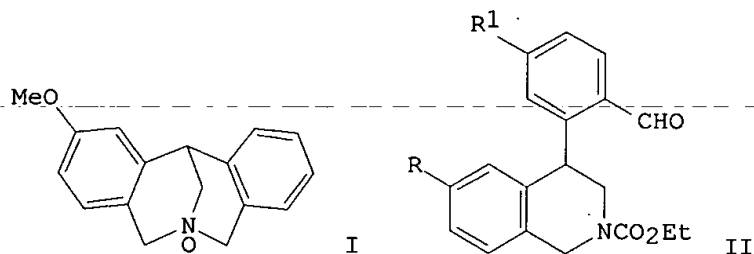
RN 67165-56-4 CAPLUS

CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl- (9CI) (CA INDEX NAME)



09/704,306

LA8 ANSWER 77 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1985:166594 CAPLUS  
DN 102:166594  
TI The control of orientation of Polonovski and the related reactions  
AU Nomoto, Takashi; Takayama, Hiroaki  
CS Fac. Pharm. Sci., Teikyo Univ., Kanagawa, 199, Japan  
SO Journal of the Chemical Society, Chemical Communications (1984), (24),  
1644-6  
CODEN: JCCCAT; ISSN: 0022-4936  
DT Journal  
LA English  
OS CASREACT 102:166594  
GI

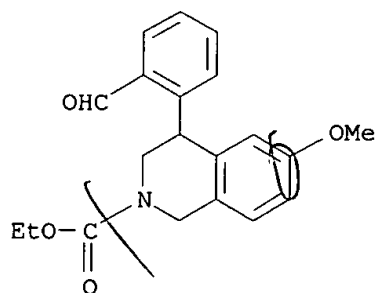


AB Treatment of tetrahydromethanodibenzazocine N-oxide I with Me<sub>3</sub>COK in Me<sub>3</sub>COH at 150.degree. for 2 h followed by Na<sub>2</sub>CO<sub>3</sub> and ClCO<sub>2</sub>Et gave 80% of an 8:1 mixt. of tetrahydroisoquinolines II [R = OMe, R<sub>1</sub> = H (III); R = H, R<sub>1</sub> = OMe (IV)], whereas reaction with (F<sub>3</sub>CSO<sub>2</sub>)<sub>2</sub>O in CH<sub>2</sub>Cl<sub>2</sub> at 0.degree. for 0.5 h followed by Na<sub>2</sub>CO<sub>3</sub> and ClCO<sub>2</sub>Et gave 89% of a 1:5 mixt. of III and IV. As the base used was stronger and the leaving group less effective, an increasing proportion of III was obtained. Similar results were obsd. for other asym. substituted N-oxides.

IT **95930-03-3P 95930-04-4P 95930-05-5P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 95930-03-3 CAPLUS

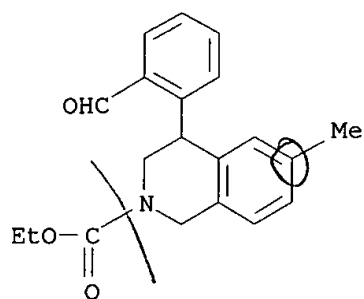
CN 2(1H)-Isoquinolinecarboxylic acid, 4-(2-formylphenyl)-3,4-dihydro-6-methoxy-, ethyl ester (9CI) (CA INDEX NAME)



RN 95930-04-4 CAPLUS

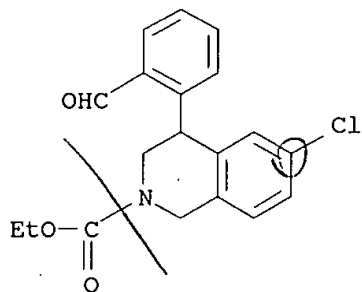
CN 2(1H)-Isoquinolinecarboxylic acid, 4-(2-formylphenyl)-3,4-dihydro-6-methyl-, ethyl ester (9CI) (CA INDEX NAME)

09/704,306

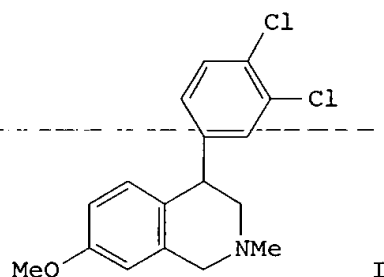


RN 95930-05-5 CAPLUS

CN 2(1H)-Isoquinolinecarboxylic acid, 6-chloro-4-(2-formylphenyl)-3,4-dihydro-  
, ethyl ester (9CI) (CA INDEX NAME)



L48 ANSWER 78 OF 100 CAPLUS COPYRIGHT 2003 ACS  
 AN 1985:39416 CAPLUS  
 DN 102:39416  
 TI Gas-liquid chromatography analysis with electron-capture detection of diclofensine in human plasma following derivatization  
 AU Hojabri, H.; Dadgar, D.; Glennon, J. D.  
 CS Dep. Chem., Univ. Coll., Cork, Ire.  
 SO Journal of Chromatography (1984), 311(1), 189-93  
 CODEN: JOCRAM; ISSN: 0021-9673  
 DT Journal  
 LA English  
 GI

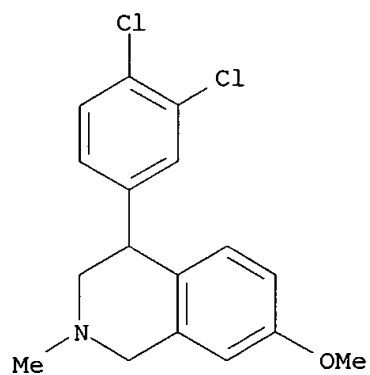


AB A gas-liq. chromatog. method for the detn. of diclofensine (I) [ **67165-56-4**] in plasma which involved solvent extn. and the formation of a fluorinated deriv. of the amine is described. Imipramine-HCl was used as the internal std. Chromatog. column was packed with 3% OV-17 on Chromosorb W HP. The oven temp. was 265.degree. with the detector and injection port temp. maintained at 300.degree.. I can be extd. from plasma at pH 9 with a no. of org. solvents. The extn. efficiency was found to be 80, 50, 72, and 75% with Et2O, CHCl3, toluene, and hexane, resp. I was first demethylated using Me chloroformate followed by hydrolysis of the urethane to N-desmethyldiclofensine [ **67165-56-4**]. The final step involved derivatization with heptafluorobutyric anhydride in the presence of triethylamine. The retention times for I and the internal std. were 2.78 and 1.96 min, resp. The coeff. of variation was 3.3% at 700 ng/mL and 6.2% at 100 ng/mL. The potential use of this method in clin. application is discussed.

IT **67165-56-4**  
 RL: ANT (Analyte); ANST (Analytical study)  
 (detn. of, in blood by gas liq. chromatog.)

RN 67165-56-4 CAPLUS

CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-  
 (9CI) (CA INDEX NAME)



RL: FORM (Formation, nonpreparative)

(formation of, as diclofenac desmethylation product, gas liq.  
chromatog. detn. in relation to

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09/704,306

~~L48~~ ANSWER 79 OF 100 CAPLUS COPYRIGHT 2003 ACS

~~AN~~ 1985:21140 CAPLUS

~~DN~~ 102:21140

~~TI~~ Latifine, a biogenetic isomer of cherylline, from *Crinum latifolium* L

~~AU~~ Kobayashi, Shigeru; Tokumoto, Toshihiro; Taira, Zenei

~~CS~~ Fac. Pharm. Sci., Tokushima Univ., Tokushima, 770, Japan

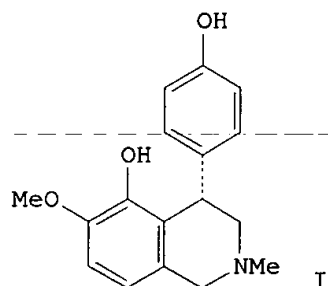
~~SO~~ Journal of the Chemical Society, Chemical Communications (1984), (15), 1043-4

CODEN: JCCCAT; ISSN: 0022-4936

~~DT~~ Journal

~~LA~~ English

~~GI~~



AB Latifine (I) was isolated from *C. latifolium* and its structure and configuration detd. by spectral methods, CD spectroscopy, and x-ray crystallog. anal.

IT **93915-33-4**

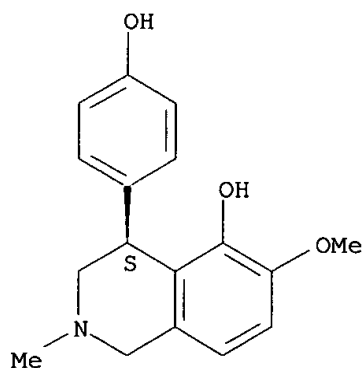
RL: BIOL (Biological study)

(from *Crinum latifolium*, crystal and mol. structure of)

RN 93915-33-4 CAPLUS

CN 5-Isoquinolinol, 1,2,3,4-tetrahydro-4-(4-hydroxyphenyl)-6-methoxy-2-methyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **93915-34-5P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

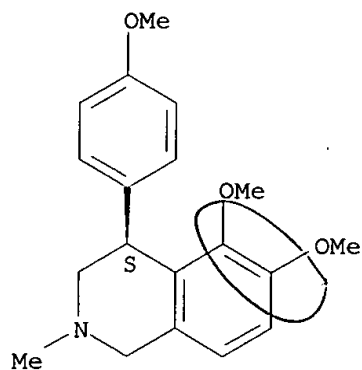
RN 93915-34-5 CAPLUS



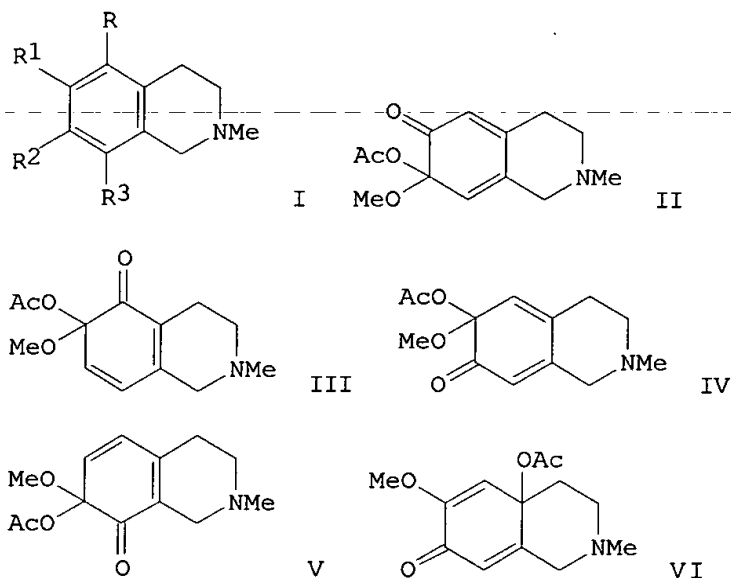
09/704,306

CN Isoquinoline, 1,2,3,4-tetrahydro-5,6-dimethoxy-4-(4-methoxyphenyl)-2-methyl-, (S)- (9CI) (CA INDEX NAME)

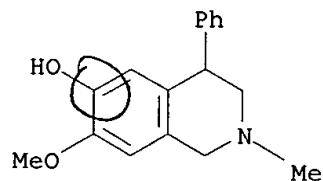
Absolute stereochemistry.



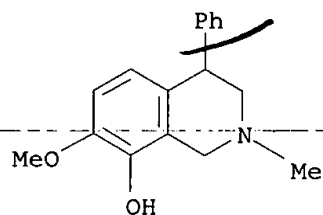
~~LI~~ 8 ANSWER 80 OF 100 CAPLUS COPYRIGHT 2003 ACS  
~~AN~~ 1984:103140 CAPLUS  
 DN 100:103140  
 TI A comment on lead tetraacetate oxidation of four guaiacol-type  
 1,2,3,4-tetrahydroisoquinolines  
 AU Hara, Hiroshi; Shinoki, Hiroshi; Hoshino, Osamu; Umezawa, Bunsuke  
 CS Fac. Pharm. Sci., Sci. Univ. Tokyo, Tokyo, 162, Japan  
 SO Heterocycles (1983), 20(11), 2149-54  
 CODEN: HTCYAM; ISSN: 0385-5414  
 DT Journal  
 LA English  
 OS CASREACT 100:103140  
 GI



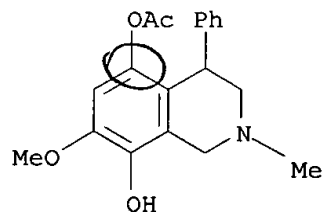
AB Pb(OAc)<sub>4</sub> oxidn. of 4 guaiacol-type isoquinolines I (R = R<sub>3</sub> = H, R<sub>1</sub> = OH, R<sub>2</sub> = MeO; R = R<sub>3</sub> = H, R<sub>1</sub> = MeO, R<sub>2</sub> = OH; R = OH, R<sub>1</sub> = MeO, R<sub>2</sub> = R<sub>3</sub> = H; R = R<sub>1</sub> = H, R<sub>2</sub> = MeO, R<sub>3</sub> = OH) at 0.degree. gave quinol acetates II-V; oxidn. of I in AcOH led to acetoxy derivs. I (R = AcO, R<sub>1</sub> = H, R<sub>2</sub> = MeO, R<sub>3</sub> = OH; R = OH, R<sub>1</sub> = MeO, R<sub>2</sub> = H, R<sub>3</sub> = AcO) and VI, which were also obtained from II-V by treatment with AcOH.  
 IT **88776-67-4 88776-68-5**  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (oxidn. of, by lead tetraacetate)  
 RN 88776-67-4 CAPLUS  
 CN 6-Isoquinolinol, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-phenyl- (9CI)  
 (CA INDEX NAME)



RN 88776-68-5 CAPLUS  
 CN 8-Isoquinolinol, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-phenyl- (9CI)  
 (CA INDEX NAME)

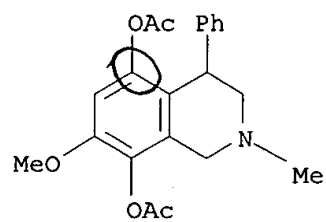


IT 88776-63-0P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (prepn. and acetylation of)  
 RN 88776-63-0 CAPLUS  
 CN 5,8-Isoquinolinediol, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-phenyl-,  
 5-acetate (9CI) (CA INDEX NAME)



IT 88776-65-2P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 RN 88776-65-2 CAPLUS  
 CN 5,8-Isoquinolinediol, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-phenyl-,  
 diacetate (ester) (9CI) (CA INDEX NAME)

09/704,306



~~143~~ ANSWER 81 OF 100 CAPLUS COPYRIGHT 2003 ACS

~~24~~ 1984:22560 CAPLUS

DN 100:22560

TI Synthesis, resolution, absolute stereochemistry, and enantioselectivity of 3',4'-dihydroxynomifensine

AU Dandridge, Penelope A.; Kaiser, Carl; Brenner, Martin; Gaitanopoulos, Dimitri; Davis, Larry D.; Webb, R. Lee; Foley, James J.; Sarau, Henry M.

CS Dep. Med. Chem., Smith Kline and French Lab., Philadelphia, PA, 19101, USA

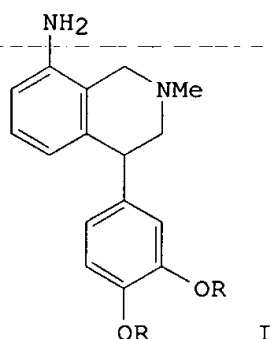
SO Journal of Medicinal Chemistry (1984), 27(1), 28-35

CODEN: JMCMAR; ISSN: 0022-2623

DT Journal

LA English

GI



AB 3',4'-Dihydroxynomifensine, (I, R = H), is an agonist of dopamine receptors in central and peripheral systems. The enantiomers of I provide addnl. probes of present conceptual models of the dopamine receptor. The racemic intermediate I (R = Me) was prepd. from 2-BrC<sub>6</sub>H<sub>4</sub>CHO and 3,4-(MeO)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CH(OH)CH<sub>2</sub>NH<sub>2</sub> in 8 steps and was resolved. Methoxyl cleavage of the isomers of I (R = Me) afforded the enantiomers of I (R = H). The abs. configuration of the enantiomers of I (R = H) was detd. by single-crystal x-ray anal. D-1 dopaminergic activity resides almost exclusively in (S)-(+)-I (R = H). An accessory binding site on the dopamine receptor(s) is suggested that differs from that advanced earlier. This accessory binding site may be specific for the D-1 subpopulation of dopamine receptors.

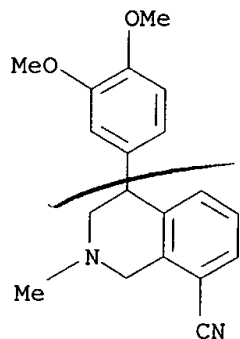
IT 87351-98-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and hydrolysis of)

RN 87351-98-2 CAPLUS

CN 8-Isoquinolinecarbonitrile, 4-(3,4-dimethoxyphenyl)-1,2,3,4-tetrahydro-2-methyl- (9CI) (CA INDEX NAME)

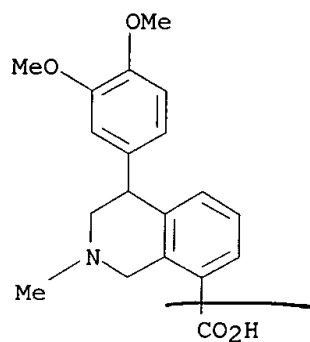


IT **87351-99-3P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(prepn. and reaction of, with azide)

RN 87351-99-3 CAPLUS

CN 8-Isoquinolinecarboxylic acid, 4-(3,4-dimethoxyphenyl)-1,2,3,4-tetrahydro-  
2-methyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

IT **87351-96-0P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(prepn. and reaction of, with cyanide)

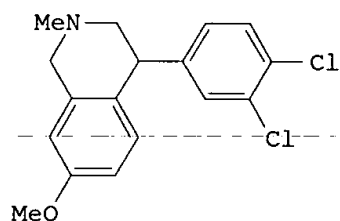
RN 87351-96-0 CAPLUS

IT **87351-97-1P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 87351-97-1 CAPLUS

L48 ANSWER 82 OF 100 CAPLUS COPYRIGHT 2003 ACS  
 AN 1983:606026 CAPLUS  
 DN 99:206026  
 TI A comparison of diclofensine and desmethyylimipramine using tyramine pressor tests in normal subjects  
 AU Jackson, S. H. D.; Turner, P.; Ehsanullah, R. S. B.  
 CS Dep. Clin. Pharmacol., St. Bartholomew's Hosp., London, EC1A 7BE, UK  
 SO British Journal of Clinical Pharmacology (1983), 16(4), 427-9  
 CODEN: BCPHBM; ISSN: 0306-5251  
 DT Journal  
 LA English  
 GI

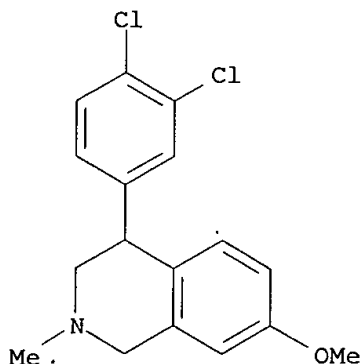


AB Eight male volunteers received placebo, diclofensine (I) [67165-56-4] 25 mg, diclofensine 50 mg, and desmethyylimipramine (DMI) [50-47-5] 50 mg at least a week apart. Using tyramine pressor tests, no statistically significant differences between the noradrenaline [51-41-2] reuptake blocking effects of the 3 active treatments could be demonstrated. Visual analog rating scales showed an increase in dryness of the mouth at 3 h after DMI but no similar effect after either dose of diclofensine.

IT 67165-56-4  
 RL: BIOL (Biological study)  
 (noradrenaline reuptake blocking by, in humans)

RN 67165-56-4 CAPLUS

CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl- (9CI) (CA INDEX NAME)



L48 ANSWER 83 OF 100 CAPLUS COPYRIGHT 2003 ACS

AN 1983:400479 CAPLUS

DN 99:479

TI A clinical pharmacological comparison of diclofensine (Ro 8-4650) with nomifensine and amitriptyline in normal human volunteers

AU Culig, J.; Ehsanullah, R. S. B.; Hallett, C.; Iliopoulou, A.; Matheson, I.; Turner, P.

CS Dep. Clin. Pharmacol., St. Bartholomew's Hosp., London, EC1A 7BE, UK

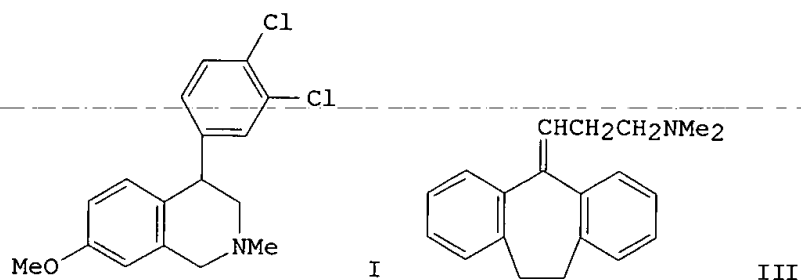
SO British Journal of Clinical Pharmacology (1983), 15(5), 537-43

CODEN: BCPHBM; ISSN: 0306-5251

DT Journal

LA English

GI



AB The pharmacodynamic profiles of single oral doses of diclofensine (I) [67165-56-4], nomifensine (II) [24526-64-5], and amitriptyline (III) [50-48-6] at 25, 50, and 50 mg, resp., were studied in healthy male volunteers in a double-blind placebo-controlled crossover study. Diclofensine did not influence salivary flow or consistently affect pupil diam. and had no significant effect on subjective measurements of sedation and mood. It had no effect on reaction time or on crit. flicker frequency. By contrast, amitriptyline significantly reduced salivary flow, produced significant sedation and impairment of mood, prolonged reaction time, and appeared to decrease crit. flicker frequency. Nomifensine significantly reduced reaction time and inhibited salivary flow. Diclofensine did not influence heart rate, blood pressure, systolic time intervals or high speed ECG. No significant treatment-related differences were obsd. in serum prolactin, cortisol, or growth hormone levels.

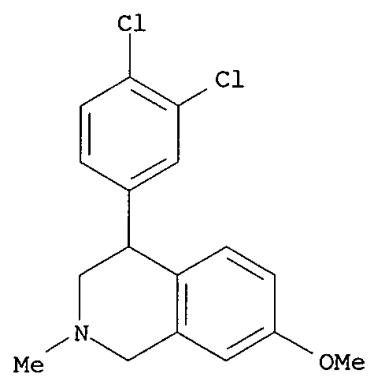
IT 67165-56-4

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(pharmacol. of, in humans)

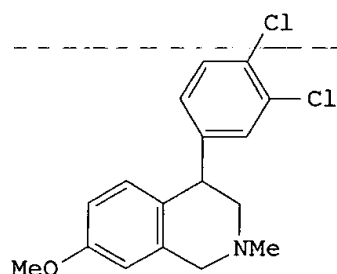
RN 67165-56-4 CAPLUS

CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-(9CI) (CA INDEX NAME)





L48 ANSWER 84 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1982:400583 CAPLUS  
DN 97:583  
TI Diclofensine (Ro 8-4650) - a potent inhibitor of monoamine uptake:  
biochemical and behavioral effects in comparison with nomifensine  
AU Keller, H. H.; Schaffner, R.; Carruba, M. O.; Burkard, W. P.; Pieri, M.;  
Bonetti, E. P.; Scherschlicht, R.; Da Prada, M.; Haefely, W. E.  
CS Pharm. Res. Dep., F. Hoffmann-La Roche and Co., Ltd., Basel, CH-4002,  
Switz.  
SO Advances in Biochemical Psychopharmacology (1982), 31(Typ. Atyp.  
Antidepressants: Mol. Mech.), 249-63  
CODEN: ABPYBL; ISSN: 0065-2229  
DT Journal  
LA English  
GI



I

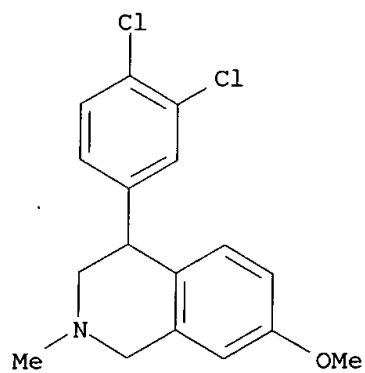
AB The antidepressant diclofensine (I) [67165-56-4] inhibits the forebrain neuronal uptake of serotonin [50-67-9], dopamine [51-61-6], and noradrenaline [51-41-2] to a similar degree. I appears to be the most effective inhibitor of dopamine uptake that is presently known. Although I is structurally similar to nomifensine it differs from this drug in that it has little or no amphetamine-like central stimulant properties, and does not induce backward locomotion behavior. These results are discussed with respect to the mechanism of the antidepressant action of I.

IT **67165-56-4**  
RL: BIOL (Biological study)  
(monoamine uptake by brain inhibition by, antidepressant activity in relation to)

RN 67165-56-4 CAPLUS

CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-  
(9CI) (CA INDEX NAME)

09/704,306



L48 ANSWER 85 OF 100 CAPLUS COPYRIGHT 2003 ACS

AN 1982:193335 CAPLUS

DN 96:193335

TI Selective suppression of rapid eye movement sleep (REMS) in cats by typical and atypical antidepressants

AU Scherschlicht, R.; Polc, P.; Schneeberger, J.; Steiner, M.; Haefely, W.

CS Pharm. Res. Dep., F. Hoffmann-La Roche and Co., Ltd., Basel, 4002, Switz.

SO Advances in Biochemical Psychopharmacology (1982), 31(Typ. Atyp.

Antidepressants: Mol. Mech.), 359-64

CODEN: ABPYBL; ISSN: 0065-2229

DT Journal

LA English

AB Typical and atypical antidepressants of various chem. classes dose-dependently suppressed rapid-eye-movement sleep (REMS) in cats without affecting nonREM-sleep (NREMS). This selectivity for REMS suppression sep'd. the antidepressants from other REMS-suppressant drugs such as d-amphetamine [51-64-9], morphine [57-27-2], or phenobarbitone [50-06-6]. The REMS suppressant property of the antidepressants was not bound to a specific mechanism of action such as monoamine oxidase inhibition, monoamine release, etc. Thus, REMS suppression may be the basic effect by which antidepressants work, however, this remains to be validated further, since REMS suppression may be representative for the antidepressant activity or is an intrinsic side effect of antidepressants in this animal model.

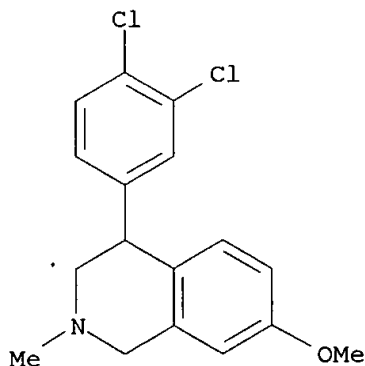
IT 67165-56-4

RL: BIOL (Biological study)

(rapid eye movement sleep response to, selective mechanism of atypical and typical antidepressants in relation to)

RN 67165-56-4 CAPLUS

CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl- (9CI) (CA INDEX NAME)



no I A  
B  
C  
D  
F

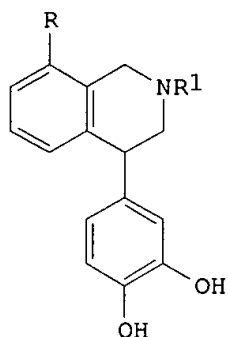
cl. 1-6, 9, 16, 18-19  
35, 36, 42

09/704,306

L48 ANSWER 86 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1982:162552 CAPLUS  
DN 96:162552  
TI 8-Substituted 4-(3,4-dihydroxyphenyl)-1,2,3,4-tetrahydroisoquinolines  
IN Brenner, L. Martin; Wardell, Joe Russell, Jr.  
PA Smithkline Corp. , USA  
SO Eur. Pat. Appl., 17 pp.  
CODEN: EPXXDW  
DT **Patent**  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 40956	A1	19811202	EP 1981-302248	19810521
	EP 40956	B1	19841031		
	R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	US 4340600	A	19820720	US 1980-152252	19800522
	JP 57016864	A2	19820128	JP 1981-74772	19810518
	AT 10091	E	19841115	AT 1981-302248	19810521
PRAI	US 1980-152252		19800522		
	EP 1981-302248		19810521		

GI



AB N-Benzylnorepinephrines were converted to title compds. I (R = OH, halo, SMe; R1 = H, Me) (and their O-alkanoyl derivs.), which showed renal vasodilator activity. Thus, 3,4-(MeO)2C6H3CH(OH)CH2NHCH2C6H4OMe-2 was treated with AlCl3, and the product was demethylated (BBr3) to give I (R = OH, R1 = H) hydrobromide.

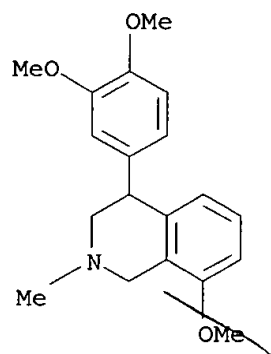
IT **81362-79-0P 81362-80-3P 81362-88-1P**  
**81362-93-8P 81362-94-9P 81362-96-1P**  
**81379-73-9P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and demethylation of)

RN 81362-79-0 CAPLUS

CN Isoquinoline, 4-(3,4-dimethoxyphenyl)-1,2,3,4-tetrahydro-8-methoxy-2-methyl- (9CI) (CA INDEX NAME)

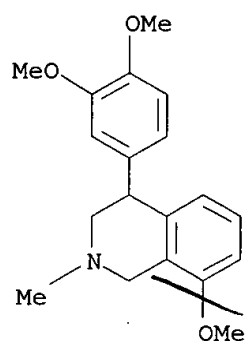
09/704,306



RN 81362-80-3 CAPLUS

CN Isoquinoline, 4-(3,4-dimethoxyphenyl)-1,2,3,4-tetrahydro-8-methoxy-2-methyl-, hydrochloride (9CI) (CA INDEX NAME)

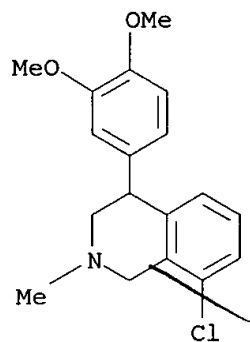
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● HCl

RN 81362-88-1 CAPLUS

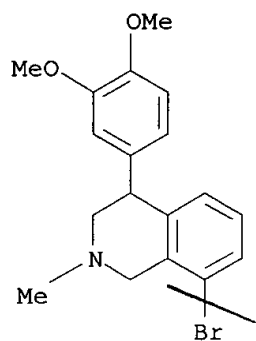
CN Isoquinoline, 8-chloro-4-(3,4-dimethoxyphenyl)-1,2,3,4-tetrahydro-2-methyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

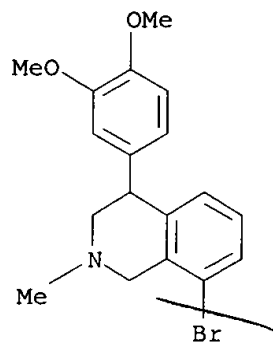
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RN 81362-93-8 CAPLUS  
 CN Isoquinoline, 8-bromo-4-(3,4-dimethoxyphenyl)-1,2,3,4-tetrahydro-2-methyl-  
 (9CI) (CA INDEX NAME)



RN 81362-94-9 CAPLUS  
 CN Isoquinoline, 8-bromo-4-(3,4-dimethoxyphenyl)-1,2,3,4-tetrahydro-2-methyl-  
 , hydrochloride (9CI) (CA INDEX NAME)

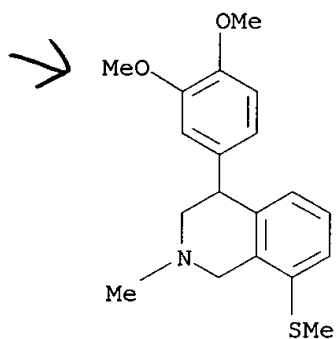
09/704,306



● HCl

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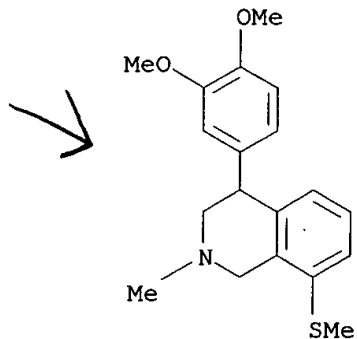
RN 81362-96-1 CAPLUS  
CN Isoquinoline, 4-(3,4-dimethoxyphenyl)-1,2,3,4-tetrahydro-2-methyl-8-(methylthio)-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 81379-73-9 CAPLUS  
CN Isoquinoline, 4-(3,4-dimethoxyphenyl)-1,2,3,4-tetrahydro-2-methyl-8-(methylthio)- (9CI) (CA INDEX NAME)

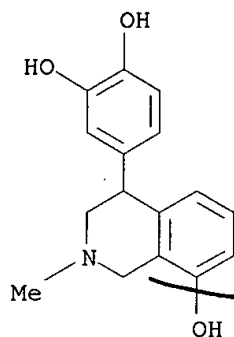




IT 81362-81-4P 81362-95-0P 81362-97-2P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and renal vasodilator activity of)

RN 81362-81-4 CAPLUS

CN 1,2-Benzenediol, 4-(1,2,3,4-tetrahydro-8-hydroxy-2-methyl-4-isoquinolinyl)-  
 , hydrobromide (9CI) (CA INDEX NAME)

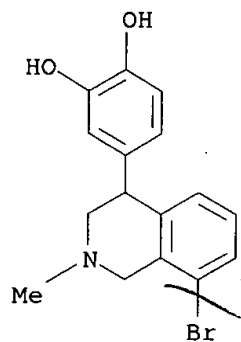


● HBr

RN 81362-95-0 CAPLUS

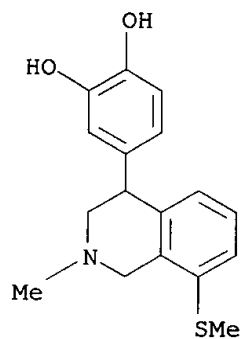
CN 1,2-Benzenediol, 4-(8-bromo-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)-,  
 hydrobromide (9CI) (CA INDEX NAME)

09/704,306



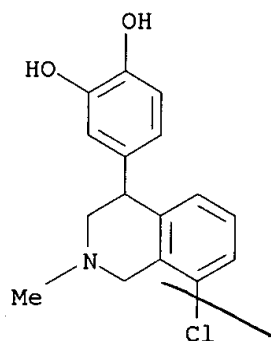
● HBr

RN 81362-97-2 CAPLUS  
CN 1,2-Benzenediol, 4-[1,2,3,4-tetrahydro-2-methyl-8-(methylthio)-4-isoquinolinyl]-, hydrobromide (9CI) (CA INDEX NAME)



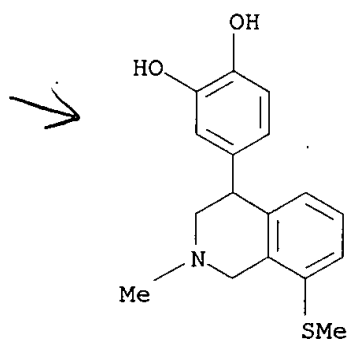
● HBr

IT 81362-89-2P 81362-98-3P 81362-99-4P  
81363-00-0P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)  
RN 81362-89-2 CAPLUS  
CN 1,2-Benzenediol, 4-(8-chloro-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl)-, hydrobromide (9CI) (CA INDEX NAME)



● HBr

RN 81362-98-3 CAPLUS  
CN 1,2-Benzenediol, 4-[1,2,3,4-tetrahydro-2-methyl-8-(methylthio)-4-isoquinolinyl]- (9CI) (CA INDEX NAME)

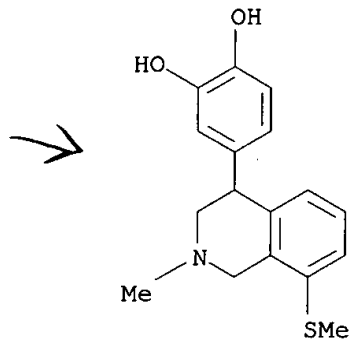


RN 81362-99-4 CAPLUS  
CN 1,2-Benzenediol, 4-[1,2,3,4-tetrahydro-2-methyl-8-(methylthio)-4-isoquinolinyl]-, methanesulfonate (salt) (9CI) (CA INDEX NAME)

CM 1

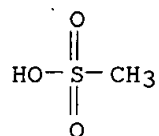
CRN 81362-98-3  
CMF C17 H19 N O2 S

09/704,306



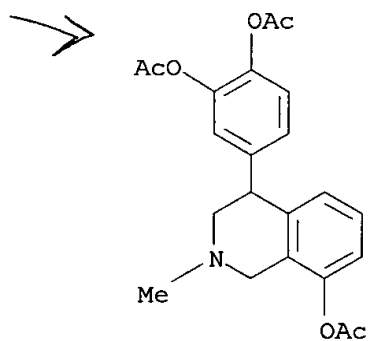
CM 2

CRN 75-75-2  
CMF C H4 O3 S



RN 81363-00-0 CAPLUS

CN 1,2-Benzenediol, 4-[8-(acetyloxy)-1,2,3,4-tetrahydro-2-methyl-4-isoquinolinyl]-, diacetate (ester), hydrobromide (9CI) (CA INDEX NAME)

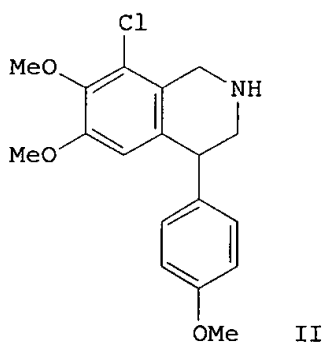
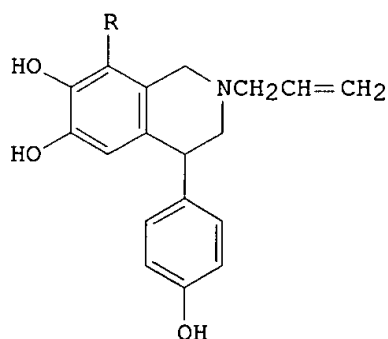


● HBr

09/704,306

LAB ANSWER 87 OF 100 CAPLUS COPYRIGHT 2003 ACS  
 AN 1982:142724 CAPLUS  
 DN 96:142724  
 TI Dopaminergic isoquinolines  
 IN Brenner, Martin L.  
 PA Smithkline Corp. , USA  
 SO Eur. Pat. Appl., 15 pp.  
 CODEN: EPXXDW  
 DT **Patent**  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 43729	A1	19820113	EP 1981-303088	19810707
	EP 43729	B1	19840201		
	R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	US 4340601	A	19820720	US 1980-166933	19800708
	JP 57062260	A2	19820415	JP 1981-104940	19810703
	DK 8103000	A	19820109	DK 1981-3000	19810707
	DK 152210	B	19880208		
	DK 152210	C	19880620		
	AT 6061	E	19840215	AT 1981-303088	19810707
PRAI	US 1980-166933		19800708		
	EP 1981-303088		19810707		
GI					



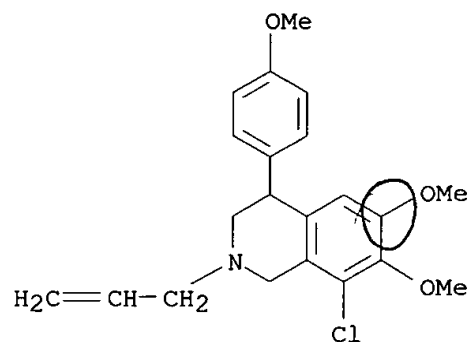
AB Isoquinolines I (R = halo) and their triesters were prepd. Thus 2,3,4-Cl(MeO)2C6H2CHO was treated with 4-MeOC6H4CH(OH)CH2NH2 to give a Schiff base which was reduced to 2,3,4-Cl(MeO)2C6H2CH2NHCH2CH(OH)C6H4OMe-4. The latter compd. was cyclized with CF3CO2H to give II. Allylation of II and demethylation gave I (R = Cl).

IT **81257-82-1P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (prepn. and demethylation of)

RN 81257-82-1 CAPLUS

CN Isoquinoline, 8-chloro-1,2,3,4-tetrahydro-6,7-dimethoxy-4-(4-methoxyphenyl)-2-(2-propenyl)- (9CI) (CA INDEX NAME)



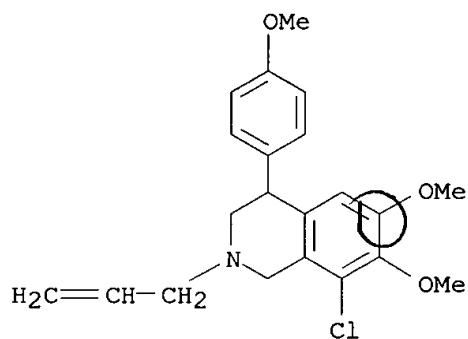
IT 81257-81-0P 81257-83-2P 81257-84-3P

81257-85-4P 81257-86-5P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 81257-81-0 CAPLUS

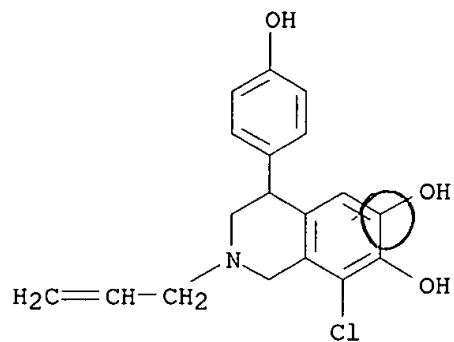
CN Isoquinoline, 8-chloro-1,2,3,4-tetrahydro-6,7-dimethoxy-4-(4-methoxyphenyl)-2-(2-propenyl)-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

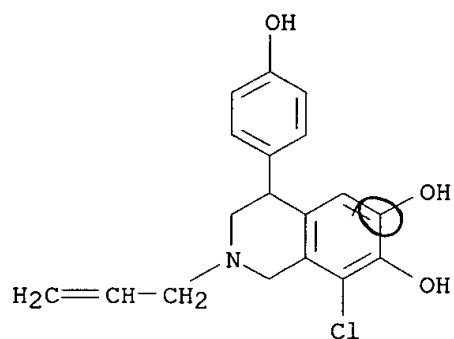
RN 81257-83-2 CAPLUS

CN 6,7-Isoquinolinediol, 8-chloro-1,2,3,4-tetrahydro-4-(4-hydroxyphenyl)-2-(2-propenyl)-, hydrobromide (9CI) (CA INDEX NAME)



● HBr

RN 81257-84-3 CAPLUS  
 CN 6,7-Isoquinolinediol, 8-chloro-1,2,3,4-tetrahydro-4-(4-hydroxyphenyl)-2-(2-propenyl)- (9CI) (CA INDEX NAME)

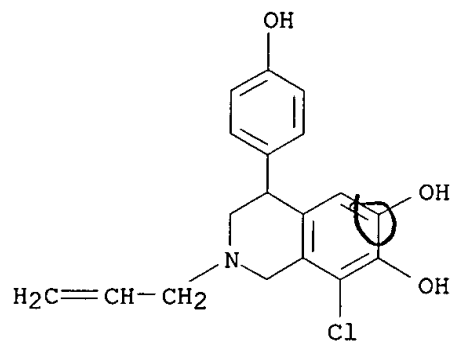


RN 81257-85-4 CAPLUS  
 CN 6,7-Isoquinolinediol, 8-chloro-1,2,3,4-tetrahydro-4-(4-hydroxyphenyl)-2-(2-propenyl)-, methanesulfonate (salt) (9CI) (CA INDEX NAME)

CM 1

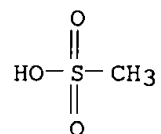
CRN 81257-84-3  
 CMF C18 H18 Cl N O3

09/704,306

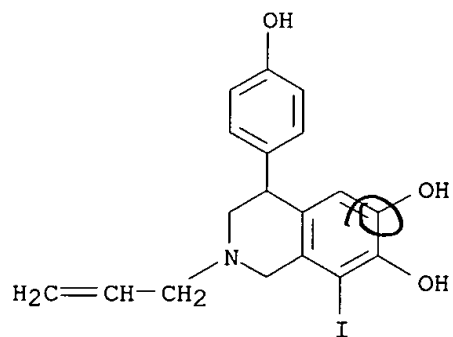


CM 2

CRN 75-75-2  
CMF C H4 O3 S



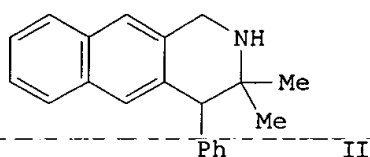
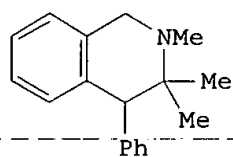
RN 81257-86-5 CAPLUS  
CN 6,7-Isoquinolinediol, 1,2,3,4-tetrahydro-4-(4-hydroxyphenyl)-8-iodo-2-(2-propenyl)- (9CI) (CA INDEX NAME)





09/704,306

✓  
148 ANSWER 88 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1981:424761 CAPLUS  
DN 95:24761  
TI Preparation of 4-aryl-1,2,3,4-tetrahydro-3,3-dimethylisoquinolines and  
1,2,3,4-tetrahydro-3,3-dimethyl-4-phenylbenz[h]isoquinolines  
AU Bobowski, George; Gottlieb, Jeffrey M.; West, Barbara  
CS Warner-Lambert Pharm. Res. Div., Ann Arbor, MI, 48105, USA  
SO Journal of Heterocyclic Chemistry (1980), 17(7), 1563-8  
CODEN: JHTCAD; ISSN: 0022-152X  
DT Journal  
LA English  
GI



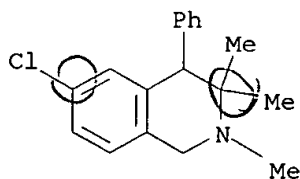
AB Synthetic procedures to prep. a no. of 4-aryl-1,2,3,4-tetrahydro-3,3-dimethylisoquinolines, e.g., I, and their benzo derivs., e.g. II, through a series of intermediates are described. The condensation of .alpha.-(1-amino-1-methylethyl)arylmethanols with arylaldehydes gave imino derivs. which on redn. with borohydride gave secondary amines, e.g. PhCH<sub>2</sub>NHMeCHPhOH. Cyclization of the amines with mineral acids gave the target compds. Antisecretory activities of the amines are briefly discussed.

IT 77740-53-5P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 77740-53-5 CAPLUS

CN Isoquinoline, 6-chloro-1,2,3,4-tetrahydro-2,3,3-trimethyl-4-phenyl- (9CI)  
(CA INDEX NAME)

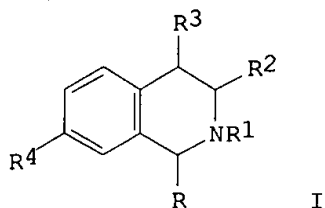


09/704,306

~~L48~~ ANSWER 89 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1977:405827 CAPLUS  
DN 87:5827  
TI Tetrahydroisoquinoline derivatives  
IN Gardner, Derek Victor  
PA Beecham Group Ltd., UK  
SO Ger. Offen., 58 pp.  
CODEN: GWXXBX  
DT Patent  
LA German  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2635276	A1	19770217	DE 1976-2635276	19760805
	BE 844783	A1	19770131	BE 1976-169475	19760730
	SE 7608641	A	19770210	SE 1976-8641	19760730
	IL 50176	A1	19791031	IL 1976-50176	19760730
	US 4113869	A	19780912	US 1976-710446	19760802
	CH 622780	A	19810430	CH 1976-10020	19760805
	DK 7603579	A	19770210	DK 1976-3579	19760806
	AT 7605868	A	19790615	AT 1976-5868	19760806
	AT 354448	B	19790110		
	CA 1076119	A1	19800422	CA 1976-258633	19760806
	NL 7608856	A	19770211	NL 1976-8856	19760809
	JP 52023083	A2	19770221	JP 1976-94721	19760809
	FR 2320755	A1	19770311	FR 1976-24258	19760809
	FR 2320755	B1	19790914		
	AU 498422	B2	19790315	AU 1976-16702	19760809
	HU 173560	P	19790628	HU 1976-BE1265	19760809
	AT 353793	B	19791210	AT 1978-7173	19781005
	AT 7807173	A	19790515		
	CH 626611	A	19811130	CH 1981-522	19810127
PRAI	GB 1975-33283		19750809		
	CH 1976-10020		19760805		
	AT 1976-5868		19781005		

GI



AB Isoquinolines I [R = R2 = H, R1 = Me, R3 = Ph, 4-CF3C6H4, 4-ClC6H4, 3-CF3C6H4, 2-naphthyl, R4 = OCH2CH2NMe2; R = R2 = H, R1 = H, CH2Ph, R3 = Ph, R4 = OCH2CH2NMe2; R = R2 = H, R1 = Me, R3 = Ph, R4 = OCH2CH2NMeCH2Ph, OCH2CH2NHMe, OCH2CH(OH)CH2NMe2; R = R1 = Me, R2 = H, R3 = Ph, R4 = OCH2CH2NMe2; R = H, R1 = R2 = Me, R3 = Ph, R4 = OCH2CH2NMe2] were prepd. by treating 7-methoxy-4-isoquinolinones with R3Li, reducing the isoquinolinols with NaBH4, demethylating I (R4 = OMe), and aminoalkylating I (R4 = OH). I are appetite depressants and antidepressants. Thus, I (R = R2 = H, R1 = Me, R3 = Ph, R4 = OCH2CH2NMe2) gave a 64% decrease in food intake at 20 mg/kg orally in rats and had a reserpine-antagonist ED50 0.03

09/704,306

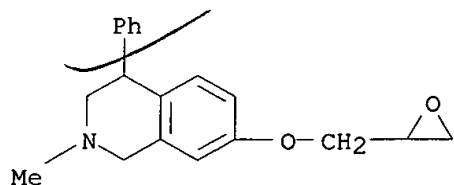
mg/kg in mice.

IT 62889-00-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(prepn. and amination of)

RN 62889-00-3 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-2-methyl-7-(oxiranylmethoxy)-4-phenyl-  
(9CI) (CA INDEX NAME)



IT 62888-67-9P 62888-68-0P 62888-69-1P

62888-70-4P 62888-71-5P 62888-73-7P

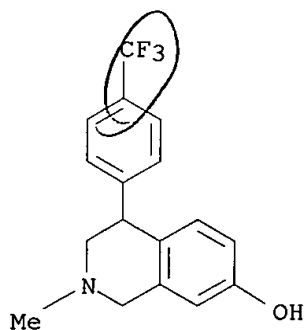
62888-92-0P 62888-97-5P 62889-03-6P

62889-04-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(prepn. and aminoalkylation of)

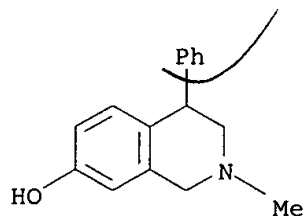
RN 62888-67-9 CAPLUS

CN 7-Isoquinolinol, 1,2,3,4-tetrahydro-2-methyl-4-[4-(trifluoromethyl)phenyl]-  
(9CI) (CA INDEX NAME)



RN 62888-68-0 CAPLUS

CN 7-Isoquinolinol, 1,2,3,4-tetrahydro-2-methyl-4-phenyl- (9CI) (CA INDEX  
NAME)



RN 62888-69-1 CAPLUS

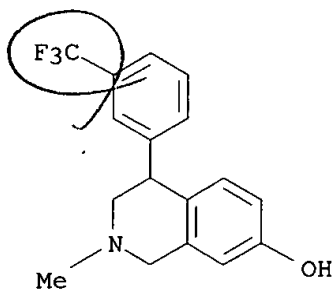
RN 62888-70-4 CAPLUS

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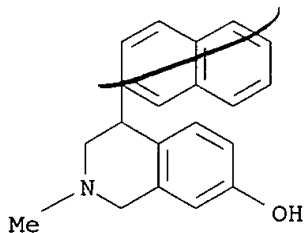
09/704,306

CN 7-Isoquinolinol, 1,2,3,4-tetrahydro-2-methyl-4-[3-(trifluoromethyl)phenyl]-  
(9CI) (CA INDEX NAME)



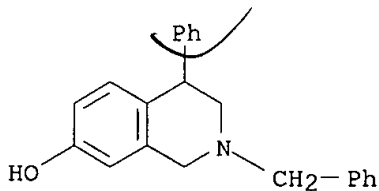
RN 62888-71-5 CAPLUS

CN 7-Isoquinolinol, 1,2,3,4-tetrahydro-2-methyl-4-(2-naphthalenyl)- (9CI)  
(CA INDEX NAME)



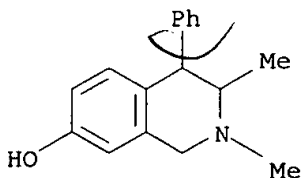
RN 62888-73-7 CAPLUS

CN 7-Isoquinolinol, 1,2,3,4-tetrahydro-4-phenyl-2-(phenylmethyl)- (9CI) (CA  
INDEX NAME)



RN 62888-92-0 CAPLUS

CN 7-Isoquinolinol, 1,2,3,4-tetrahydro-2,3-dimethyl-4-phenyl- (9CI) (CA  
INDEX NAME)

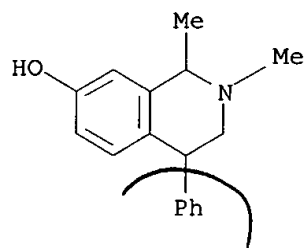


RN 62888-97-5 CAPLUS

CN 7-Isoquinolinol, 1,2,3,4-tetrahydro-1,2-dimethyl-4-phenyl- (9CI) (CA

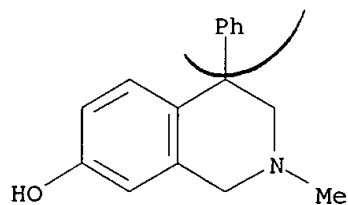
09/704,306

INDEX NAME)



RN 62889-03-6 CAPLUS  
CN 7-Isoquinolinol, 1,2,3,4-tetrahydro-2-methyl-4-phenyl-, hydrochloride,  
(+)- (9CI) (CA INDEX NAME)

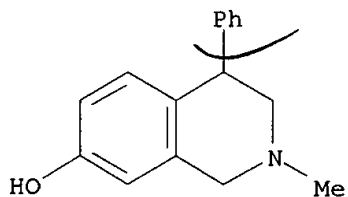
Rotation (+).



● HCl

RN 62889-04-7 CAPLUS  
CN 7-Isoquinolinol, 1,2,3,4-tetrahydro-2-methyl-4-phenyl-, hydrochloride,  
(-)- (9CI) (CA INDEX NAME)

Rotation (-).



● HCl

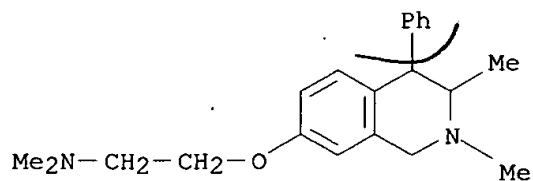
IT **62888-94-2P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and anitdepressant activity of)  
RN 62888-94-2 CAPLUS  
CN Ethanamine, N,N-dimethyl-2-[(1,2,3,4-tetrahydro-2,3-dimethyl-4-phenyl-7-  
isoquinolinyl)oxy]-, (2R,3R)-2,3-dihydroxybutanedioate (1:2) (9CI) (CA  
INDEX NAME)

09/704,306

CM 1

CRN 62888-93-1

CMF C21 H28 N2 O

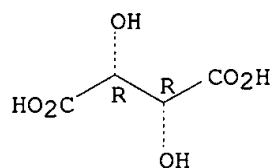


CM 2

CRN 87-69-4

CMF C4 H6 O6

Absolute stereochemistry.



IT 62888-74-8P 62888-78-2P 62888-80-6P

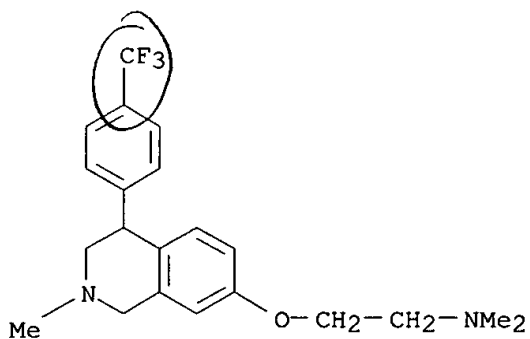
62888-99-7P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. and antidepressant and appetite depressant activity of)

RN 62888-74-8 CAPLUS

CN Ethanamine, N,N-dimethyl-2-[[1,2,3,4-tetrahydro-2-methyl-4-[4-(trifluoromethyl)phenyl]-7-isoquinolinyl]oxy]-, dihydrobromide (9CI) (CA INDEX NAME)



● 2 HBr

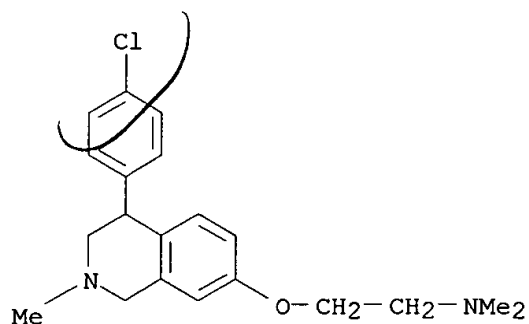
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09/704,306

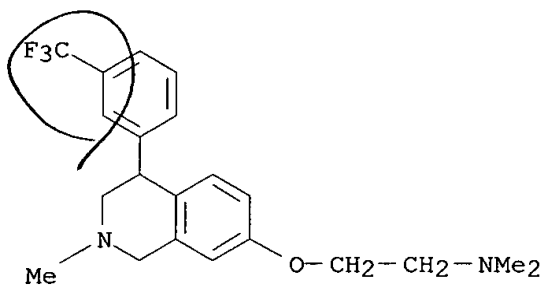
RN 62888-78-2 CAPLUS

CN Ethanamine, 2-[[4-(4-chlorophenyl)-1,2,3,4-tetrahydro-2-methyl-7-isoquinolinyl]oxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)



RN 62888-80-6 CAPLUS

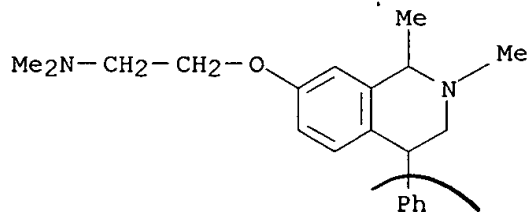
CN Ethanamine, N,N-dimethyl-2-[[1,2,3,4-tetrahydro-2-methyl-4-[3-(trifluoromethyl)phenyl]-7-isoquinolinyl]oxy]-, dihydrobromide (9CI) (CA INDEX NAME)



● 2 HBr

RN 62888-99-7 CAPLUS

CN Ethanamine, N,N-dimethyl-2-[(1,2,3,4-tetrahydro-1,2-dimethyl-4-phenyl-7-isoquinolinyl)oxy]-, dihydrobromide (9CI) (CA INDEX NAME)



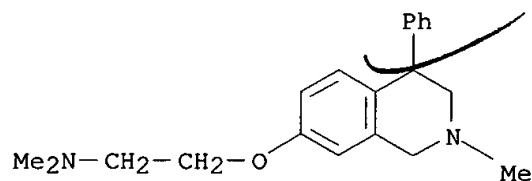
● 2 HBr

IT 62888-77-1P 62888-82-8P 62888-86-2P  
62888-88-4P 62889-02-5P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and appetite depressant activity of)

RN 62888-77-1 CAPLUS

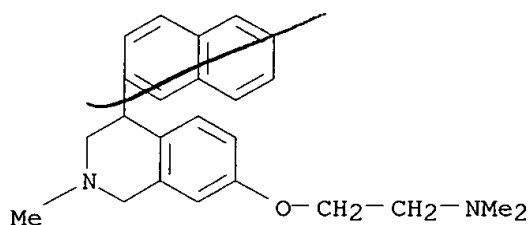
CN Ethanamine, N,N-dimethyl-2-[(1,2,3,4-tetrahydro-2-methyl-4-phenyl-7-isoquinolinyl)oxy]-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

RN 62888-82-8 CAPLUS

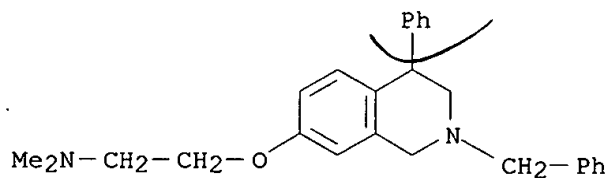
CN Ethanamine, N,N-dimethyl-2-[[1,2,3,4-tetrahydro-2-methyl-4-(2-naphthalenyl)-7-isoquinolinyl]oxy]-, dihydrobromide (9CI) (CA INDEX NAME)



● 2 HBr

RN 62888-86-2 CAPLUS

CN Ethanamine, N,N-dimethyl-2-[[1,2,3,4-tetrahydro-4-phenyl-2-(phenylmethyl)-7-isoquinolinyl]oxy]-, dihydrochloride (9CI) (CA INDEX NAME)



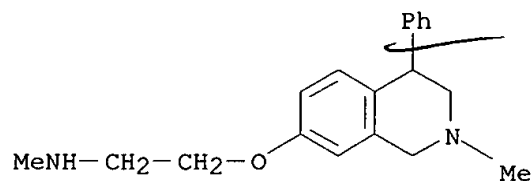
● 2 HCl

RN 62888-88-4 CAPLUS



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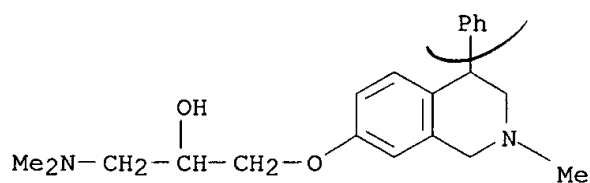
CN Ethanamine, N-methyl-2-[(1,2,3,4-tetrahydro-2-methyl-4-phenyl-7-isoquinolinyl)oxy]-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

RN 62889-02-5 CAPLUS

CN 2-Propanol, 1-(dimethylamino)-3-[(1,2,3,4-tetrahydro-2-methyl-4-phenyl-7-isoquinolinyl)oxy]-, dihydrobromide (9CI) (CA INDEX NAME)



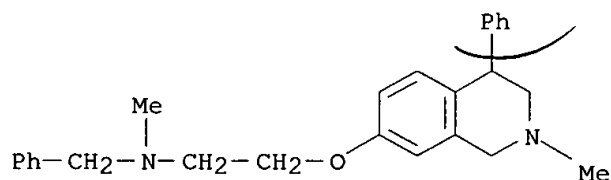
● 2 HBr

IT 62888-87-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and debenzylation of)

RN 62888-87-3 CAPLUS

CN Benzenemethanamine, N-methyl-N-[2-[(1,2,3,4-tetrahydro-2-methyl-4-phenyl-7-isoquinolinyl)oxy]ethyl]- (9CI) (CA INDEX NAME)



IT 28102-56-9P 28102-58-1P 59645-78-2P

62888-55-5P 62888-56-6P 62888-58-8P

62888-59-9P 62888-61-3P 62888-91-9P

62888-96-4P

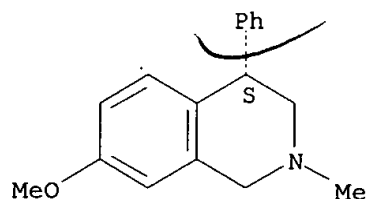
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and demethylation of)

RN 28102-56-9 CAPLUS

09/704,306

CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-phenyl-, (S)- (8CI, 9CI) (CA INDEX NAME)

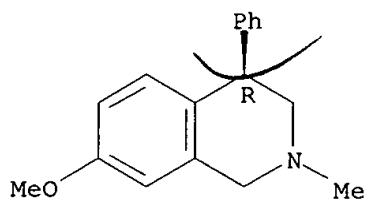
Absolute stereochemistry.



RN 28102-58-1 CAPLUS

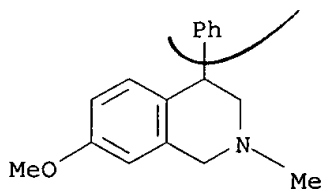
CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-phenyl-, (R)- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



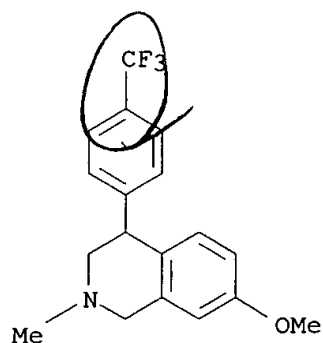
RN 59645-78-2 CAPLUS.

CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-phenyl- (9CI) (CA INDEX NAME)

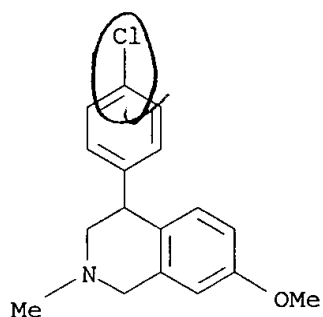


RN 62888-55-5 CAPLUS

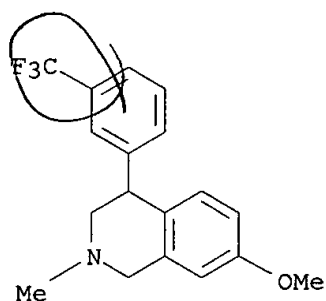
CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



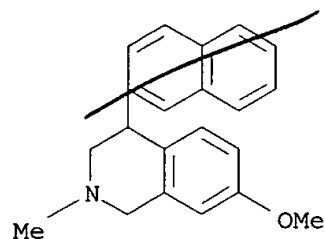
RN 62888-56-6 CAPLUS  
CN Isoquinoline, 4-(4-chlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-  
(9CI) (CA INDEX NAME)



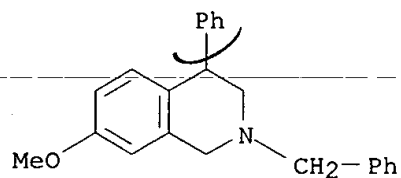
RN 62888-58-8 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-[3-  
(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



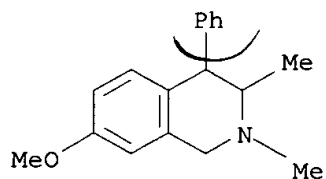
RN 62888-59-9 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-(2-naphthalenyl)-  
(9CI) (CA INDEX NAME)



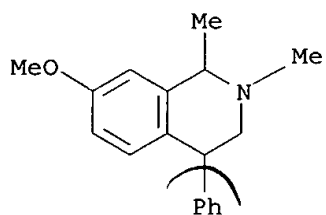
RN 62888-61-3 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-4-phenyl-2-(phenylmethyl)-  
(9CI) (CA INDEX NAME)



RN 62888-91-9 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-2,3-dimethyl-4-phenyl- (9CI)  
(CA INDEX NAME)



RN 62888-96-4 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-1,2-dimethyl-4-phenyl- (9CI)  
(CA INDEX NAME)



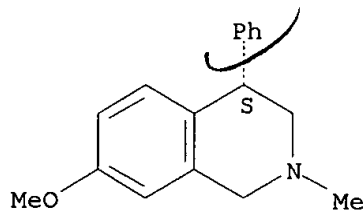
IT 28102-57-0P 37624-27-4P 62888-57-7P  
62888-75-9P 62888-76-0P 62888-79-3P  
62888-81-7P 62888-85-1P 62888-93-1P  
62888-98-6P 62889-01-4P 62889-05-8P  
62889-06-9P

RL: SPN (Synthetic preparation); PREP (Preparation)

09/704,306

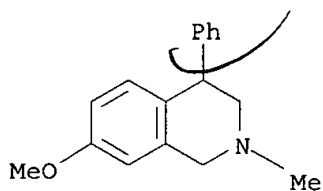
(prepn. of)  
RN 28102-57-0 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-phenyl-,  
hydrochloride, (S)- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



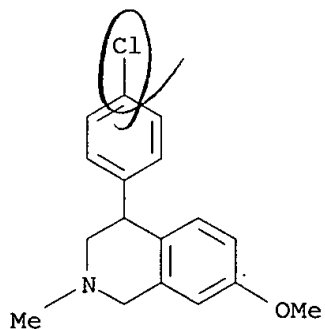
● HCl

RN 37624-27-4 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-phenyl-,  
hydrochloride (9CI) (CA INDEX NAME)



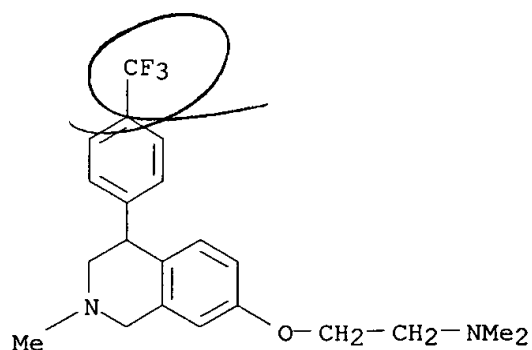
● HCl

RN 62888-57-7 CAPLUS  
CN Isoquinoline, 4-(4-chlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-,  
dihydrochloride (9CI) (CA INDEX NAME)

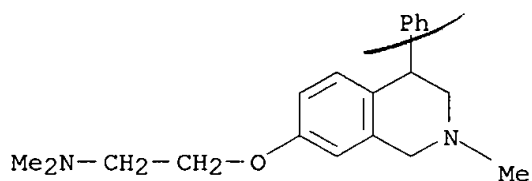


2 HCl

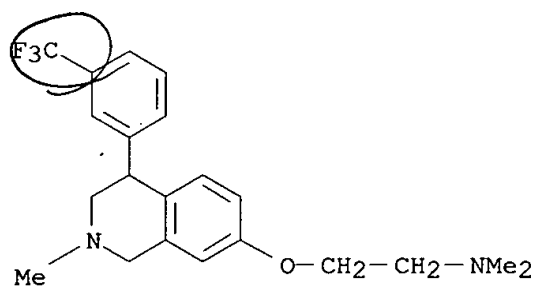
RN 62888-75-9 CAPLUS  
 CN Ethanamine, N,N-dimethyl-2-[[1,2,3,4-tetrahydro-2-methyl-4-[4-(trifluoromethyl)phenyl]-7-isoquinolinyl]oxy]- (9CI) (CA INDEX NAME)



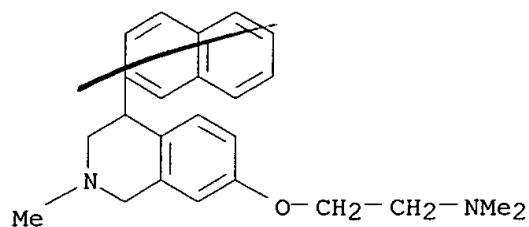
RN 62888-76-0 CAPLUS  
 CN Ethanamine, N,N-dimethyl-2-[(1,2,3,4-tetrahydro-2-methyl-4-phenyl-7-isoquinolinyl)oxy]- (9CI) (CA INDEX NAME)



RN 62888-79-3 CAPLUS  
 CN Ethanamine, N,N-dimethyl-2-[[1,2,3,4-tetrahydro-2-methyl-4-[3-(trifluoromethyl)phenyl]-7-isoquinolinyl]oxy]- (9CI) (CA INDEX NAME)

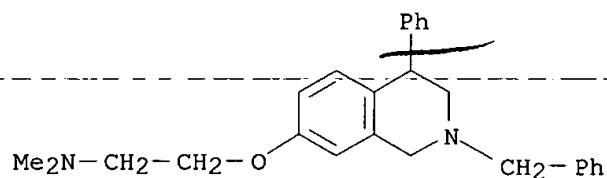


RN 62888-81-7 CAPLUS  
 CN Ethanamine, N,N-dimethyl-2-[[1,2,3,4-tetrahydro-2-methyl-4-(2-naphthalenyl)-7-isoquinolinyl]oxy]- (9CI) (CA INDEX NAME)



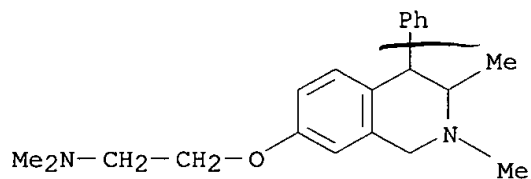
RN 62888-85-1 CAPLUS

CN Ethanamine, N,N-dimethyl-2-[[1,2,3,4-tetrahydro-4-phenyl-2-(phenylmethyl)-7-isoquinolinyl]oxy]- (9CI) (CA INDEX NAME)



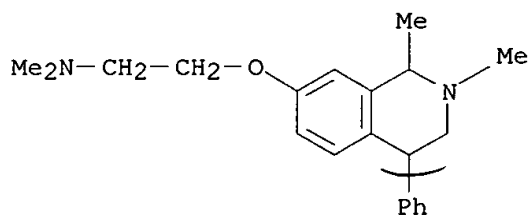
RN 62888-93-1 CAPLUS

CN Ethanamine, N,N-dimethyl-2-[(1,2,3,4-tetrahydro-2,3-dimethyl-4-phenyl-7-isoquinolinyl)oxy]- (9CI) (CA INDEX NAME)



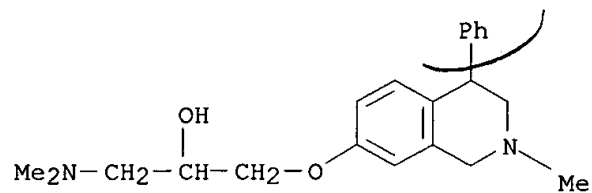
RN 62888-98-6 CAPLUS

CN Ethanamine, N,N-dimethyl-2-[(1,2,3,4-tetrahydro-1,2-dimethyl-4-phenyl-7-isoquinolinyl)oxy]- (9CI) (CA INDEX NAME)



RN 62889-01-4 CAPLUS

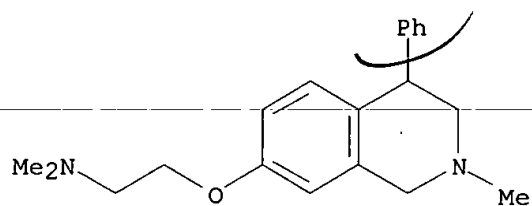
CN 2-Propanol, 1-(dimethylamino)-3-[(1,2,3,4-tetrahydro-2-methyl-4-phenyl-7-isoquinolinyl)oxy]- (9CI) (CA INDEX NAME)



RN 62889-05-8 CAPLUS

CN Ethanamine, N,N-dimethyl-2-[(1,2,3,4-tetrahydro-2-methyl-4-phenyl-7-isoquinolinyl)oxy]-, dihydrochloride, (+)- (9CI) (CA INDEX NAME)

Rotation (+).

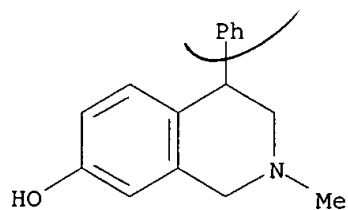


●2 HCl

RN 62889-06-9 CAPLUS

CN 7-Isoquinolinol, 1,2,3,4-tetrahydro-2-methyl-4-phenyl-, dihydrochloride, (-)- (9CI) (CA INDEX NAME)

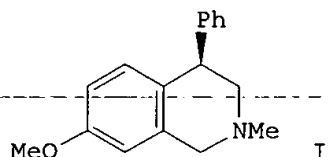
Rotation (-).



●2 HCl



~~DI~~ ANSWER 90 OF 100 CAPLUS COPYRIGHT 2003 ACS  
~~AN~~ 1976:432149 CAPLUS  
DN 85:32149  
TI Solvent and pH effects on the sign of the ORD spectrum of  
N-methyl-4-phenyl-7-methoxy-1,2,3,4-tetrahydroisoquinoline in the visible  
spectral range  
AU Toome, V.; Reymond, G.  
CS Chem. Res. Dep., Hoffmann-La Roche Inc., Nutley, NJ, USA  
SO Spectroscopy Letters (1975), 8(8), 595-8  
CODEN: SPLEBX; ISSN: 0038-7010  
DT Journal  
LA English  
GI

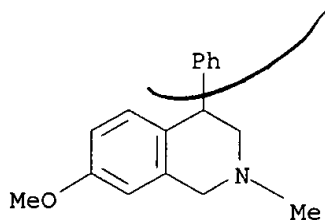


AB The solvent effect on the ORD of the title compd. (I) at 300-700 nm influenced the neg. rotational intensity but not the sign of rotation of the 1st Cotton effect at the Na D line. The ORD sign of I was reversed in 0.1N HCl-MeOH due to the proximity of the amine moiety to the sym. center. The acidities of protonated I, detd. by polarimetric and potentiometric titrns., agreed.

IT **59645-78-2**  
RL: PRP (Properties)  
(ORD of, solvent and pH effects on)

RN 59645-78-2 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-phenyl- (9CI) (CA INDEX NAME)



09/704,306

LAB ANSWER 91 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1975:409819 CAPLUS  
DN 83:9819  
TI 2-Methyl-3-substituted-4-aryl isoquinolines  
IN Houlihan, William J.; Nadelson, Jeffrey  
PA Sandoz-Wander, Inc., USA  
SO U.S., 8 pp.  
CODEN: USXXAM  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 3870722	A	19750311	US 1973-412132	19731102
PRAI	US 1973-412132		19731102		

GI For diagram(s), see printed CA Issue.

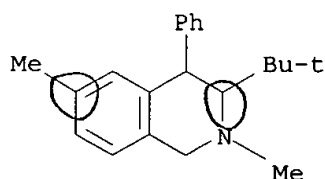
AB Four hypocholesterlemic (no data) isoquinolines I (R1 = tert-Bu, R2 = H, Me, MeO; R1 = 1-methylcyclohexyl, R2 = H) were prepd. by HCO2H-HCHO methylation of II. II(R1 = tert-Bu, R2 = H) was prepd. from BzNHMe and BzH via o-HOCHPhC6H4CONHMe, phthalide III, o-PhCH2C6H4CO2H, o-PhCH2C6H4COCl, o-PhCH2C6H4CONHMe3, o-PhCH(COCMe3)C6H4CONHMe3, isocarbostyryl IV, chloroisoquinoline V, and isoquinoline VI.

IT 55810-68-9P 55810-69-0P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

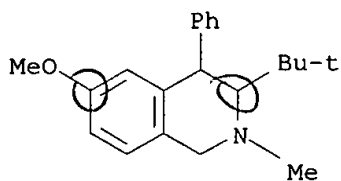
RN 55810-68-9 CAPLUS

CN Isoquinoline, 3-(1,1-dimethylethyl)-1,2,3,4-tetrahydro-2,6-dimethyl-4-phenyl- (9CI) (CA INDEX NAME)



RN 55810-69-0 CAPLUS

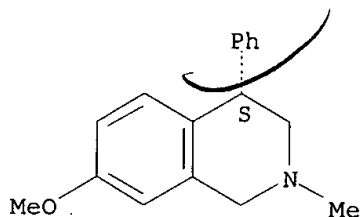
CN Isoquinoline, 3-(1,1-dimethylethyl)-1,2,3,4-tetrahydro-6-methoxy-2-methyl-4-phenyl- (9CI) (CA INDEX NAME)



09/704,306

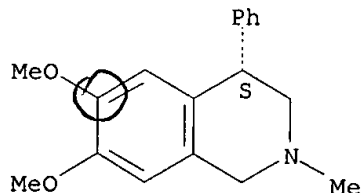
~~LAB~~ ANSWER 92 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1975:139142 CAPLUS  
DN 82:139142  
TI Application of aromatic chirality method for the determination of the absolute configuration of 4-phenyl-1,2,3,4-tetrahydroisoquinolines  
AU Toome, V.  
CS Chem. Res. Dep., Hoffmann-La Roche Inc., Nutley, NJ, USA  
SO Spectroscopy Letters (1975), 8(1), 1-5  
CODEN: SPLEBX; ISSN: 0038-7010  
DT Journal  
LA English  
GI For diagram(s), see printed CA Issue.  
AB The CD spectra of (S)-I (R = Me, H; R1, R2, R3 = H, MeO) exhibit exciton splitting in the 1Lb and 1B transitions. As the first of the split Cotton effects of (S)-I are neg., the 2 noncoplanar arom. chromophores must have left-handed, or neg., chirality on the basis of the arom. chirality method.  
IT 28102-56-9 55178-75-1  
RL: PRP (Properties)  
-----  
(CD spectrum of)  
RN 28102-56-9 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-phenyl-, (S)- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 55178-75-1 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-6,7-dimethoxy-2-methyl-4-phenyl-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



09/704,306

L48 ANSWER 93 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1973:536996 CAPLUS \\  
DN 79:136996  
TI Isoquinoline derivatives  
IN Rheiner, Alfred, Jr.  
PA Hoffmann-La Roche, F., und Co., A.-G.  
SO Patentschrift (Switz.), 13 pp. Division of Swiss 527,194 (See Ger.  
2,062,001 CA 75;129683c).  
CODEN: SWXXAS

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CH 538477	A	19730815	CH 1972-10118	19700106
PRAI	CH 1972-10118		19700106		

GI For diagram(s), see printed CA Issue.

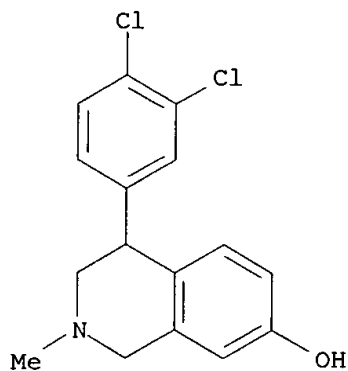
AB 4-Aryltetrahydroisoquinolines I (R = H, Me; R1 = Me, Et, CHMe2, CH2Ph; R2 = H, Cl, NO2, NH2; R3 = Cl, NO2, NH2; R4 = H, OH, OMe; R5 = OH, OMe) were prepd. Thus, 4-ClC6H4CHO was converted to its cyanohydrin, reduced to 4-ClC6H4CH(OH)CH2NH2, treated with 3-MeOC6H4CHO, followed by redn. to give 4-ClC6H4CH(OH)CH2NHCH2C6H4OMe-3. Cyclization with H2SO4 gave I (R = R1 = R2 = R4 = H, R3 = Cl, R5 = OMe), which was treated with H2CO and reduced to I (R = R2 = R4 = H, R1 = Me, R3 = Cl, R5 = OMe). Ether cleavage with HBr gave I (R = R2 = R4 = H, R1 = Me, R3 = Cl, R5 = OH) which had 114% of the antidepressant activity of amitriptyline.

IT 34041-51-5P 34041-52-6P 34041-53-7P  
34041-54-8P 34041-59-3P 34041-60-6P  
34041-61-7P 34041-65-1P 34041-66-2P  
34041-67-3P 34041-70-8P 34041-71-9P  
34041-73-1P 34041-77-5P 34041-78-6P  
34041-83-3P 34041-84-4P 34047-49-9P  
34047-53-5P 34047-54-6P 34047-60-4P  
34048-13-0P 34048-18-5P 34048-19-6P  
34048-20-9P 34048-21-0P 34048-22-1P  
34048-23-2P 34154-25-1P 34154-26-2P  
43072-81-7P 43072-87-3P 43072-88-4P  
43072-98-6P 43073-00-3P 43073-01-4P  
43170-70-3P 43170-71-4P 50560-38-8P  
50560-45-7P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

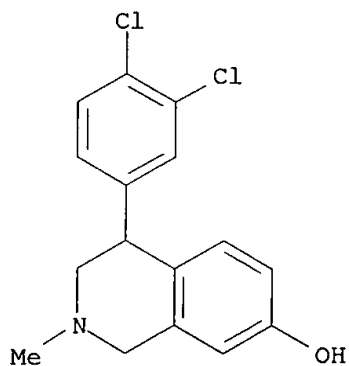
RN 34041-51-5 CAPLUS

CN 7-Isoquinolinol, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-2-methyl-,  
hydrobromide (8CI, 9CI) (CA INDEX NAME)

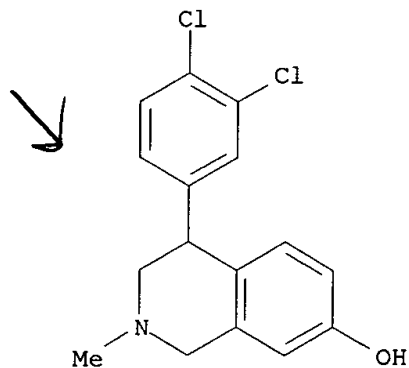


● HBr

RN 34041-52-6 CAPLUS  
CN 7-Isoquinolinol, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-2-methyl- (8CI, 9CI) (CA INDEX NAME)

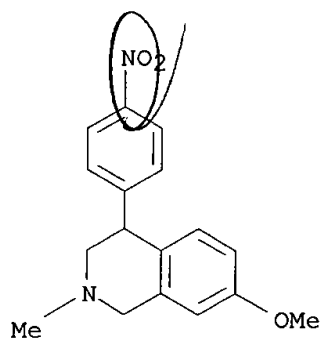


RN 34041-53-7 CAPLUS  
CN 7-Isoquinolinol, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-2-methyl-, hydrochloride (8CI, 9CI) (CA INDEX NAME)



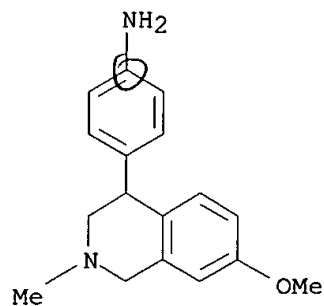
● HCl

RN 34041-54-8 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-(4-nitrophenyl)-, hydrochloride (9CI) (CA INDEX NAME)



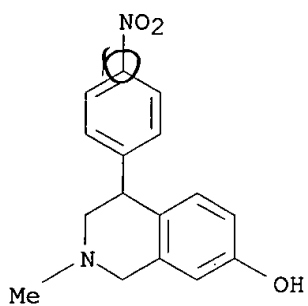
● HCl

RN 34041-59-3 CAPLUS  
CN Benzenamine, 4-(1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-isoquinolinyl)-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

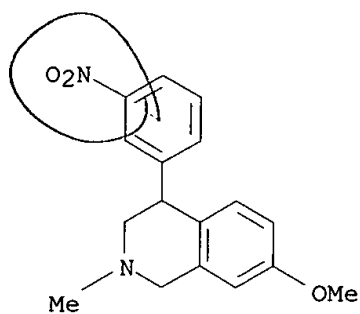
RN 34041-60-6 CAPLUS  
CN 7-Isoquinolinol, 1,2,3,4-tetrahydro-2-methyl-4-(4-nitrophenyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 34041-61-7 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-(3-nitrophenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

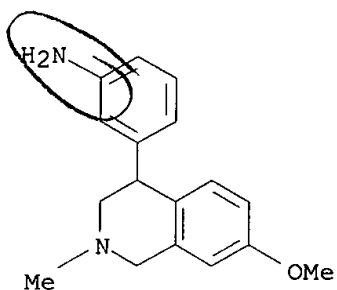
09/704,306



● HCl

RN 34041-65-1 CAPLUS

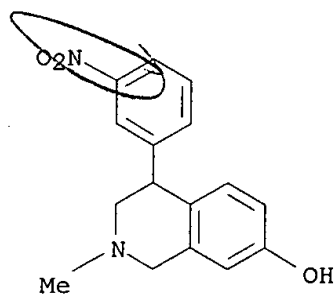
CN Benzenamine, 3-(1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-isoquinolinyl)-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 34041-66-2 CAPLUS

CN 7-Isoquinolinol, 1,2,3,4-tetrahydro-2-methyl-4-(3-nitrophenyl)-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

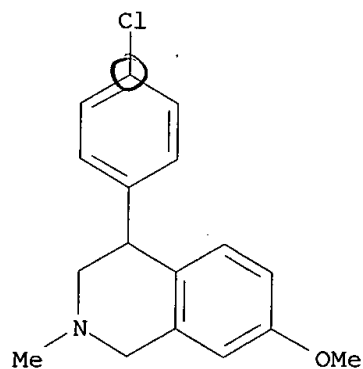
RN 34041-67-3 CAPLUS

CN Isoquinoline, 4-(4-chlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-, hydrochloride (9CI) (CA INDEX NAME)



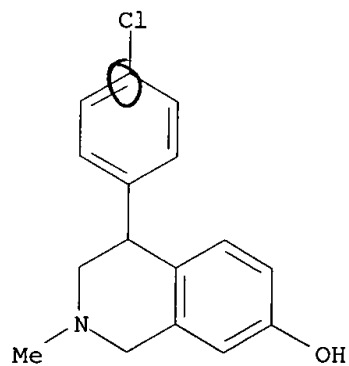
09/704,306

hydrochloride (9CI) (CA INDEX NAME)



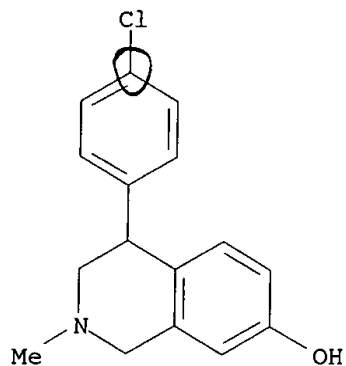
● HCl

RN 34041-70-8 CAPLUS  
CN 7-Isoquinolinol, 4-(4-chlorophenyl)-1,2,3,4-tetrahydro-2-methyl-,  
hydrobromide (9CI) (CA INDEX NAME)

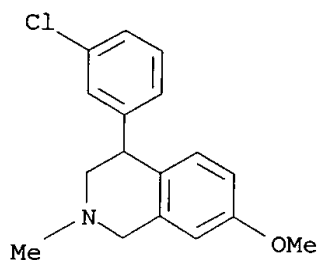


● HBr

RN 34041-71-9 CAPLUS  
CN 7-Isoquinolinol, 4-(4-chlorophenyl)-1,2,3,4-tetrahydro-2-methyl- (9CI)  
(CA INDEX NAME)

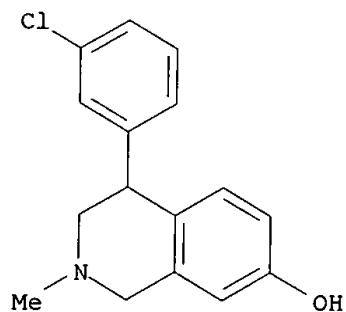


RN 34041-73-1 CAPLUS  
CN Isoquinoline, 4-(3-chlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 34041-77-5 CAPLUS  
CN 7-Isoquinolinol, 4-(3-chlorophenyl)-1,2,3,4-tetrahydro-2-methyl-, hydrochloride (9CI) (CA INDEX NAME)

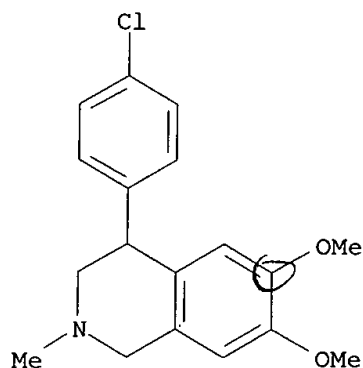


● HCl

09/704,306

RN 34041-78-6 CAPLUS

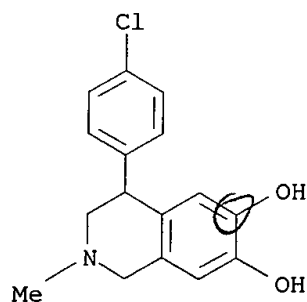
CN Isoquinoline, 4-(4-chlorophenyl)-1,2,3,4-tetrahydro-6,7-dimethoxy-2-methyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 34041-83-3 CAPLUS

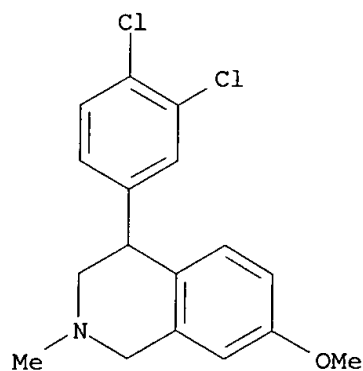
CN 6,7-Isoquinolinediol, 4-(4-chlorophenyl)-1,2,3,4-tetrahydro-2-methyl-, hydrobromide (9CI) (CA INDEX NAME)



● HBr

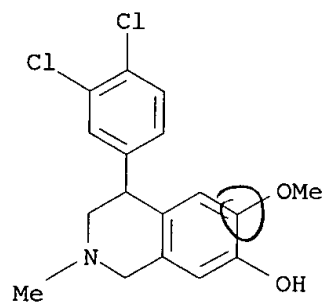
RN 34041-84-4 CAPLUS

CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-, hydrochloride (8CI, 9CI) (CA INDEX NAME)



● HCl

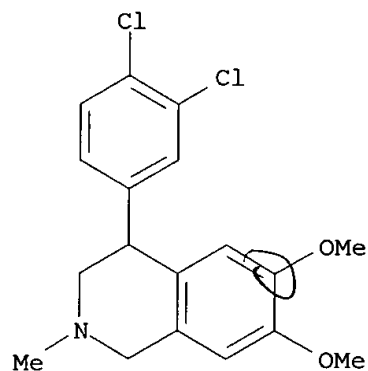
RN 34047-49-9 CAPLUS  
CN 7-Isoquinolinol, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-6-methoxy-2-methyl-, hydrochloride (8CI, 9CI) (CA INDEX NAME)



● HCl

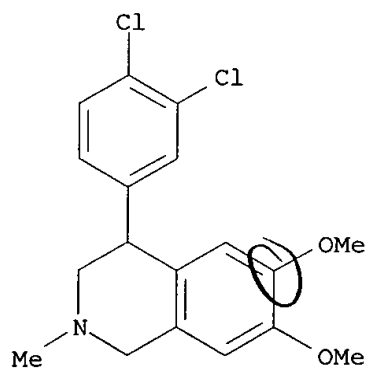
RN 34047-53-5 CAPLUS  
CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-6,7-dimethoxy-2-methyl-, hydrochloride (8CI, 9CI) (CA INDEX NAME)

09/704,306



● HCl

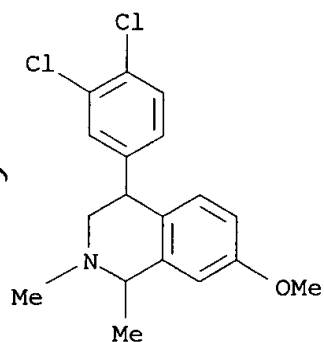
RN 34047-54-6 CAPLUS  
CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-6,7-dimethoxy-2-methyl- (8CI, 9CI) (CA INDEX NAME)



RN 34047-60-4 CAPLUS  
CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-1,2-dimethyl-, 2-hydroxy-1,2,3-propanetricarboxylate (9CI) (CA INDEX NAME)

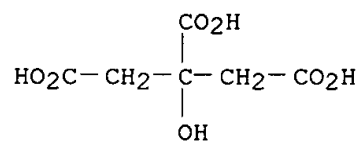
CM 1

CRN 47205-36-7  
CMF C18 H19 Cl2 N O



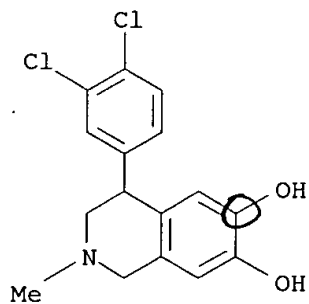
CM 2

CRN 77-92-9  
CMF C6 H8 O7



RN 34048-13-0 CAPLUS

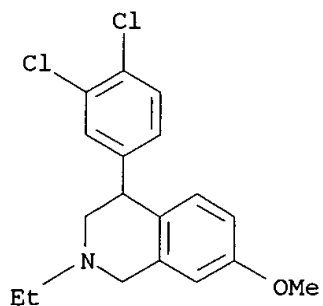
CN 6,7-Isoquinolinediol, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-2-methyl-,  
hydrobromide (8CI, 9CI) (CA INDEX NAME)



● HBr

RN 34048-18-5 CAPLUS

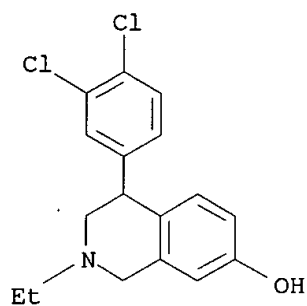
CN Isoquinoline, 4-(3,4-dichlorophenyl)-2-ethyl-1,2,3,4-tetrahydro-7-methoxy-,  
hydrochloride (8CI, 9CI) (CA INDEX NAME)



● HCl

RN 34048-19-6 CAPLUS

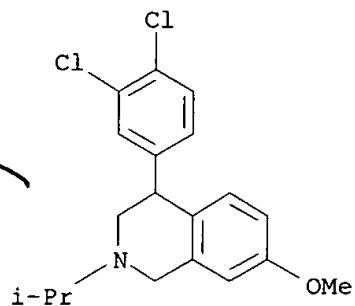
CN 7-Isoquinolinol, 4-(3,4-dichlorophenyl)-2-ethyl-1,2,3,4-tetrahydro-, hydrochloride (8CI, 9CI) (CA INDEX NAME)



● HCl

RN 34048-20-9 CAPLUS

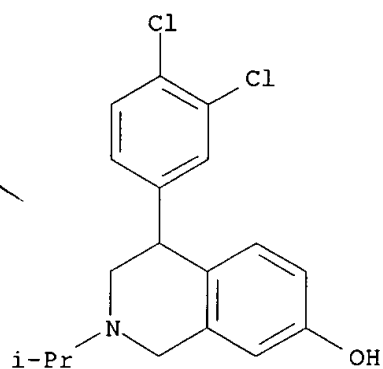
CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-(1-methylethyl)-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 34048-21-0 CAPLUS

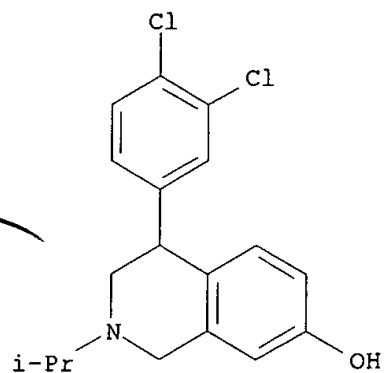
CN 7-Isoquinolinol, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-2-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 34048-22-1 CAPLUS

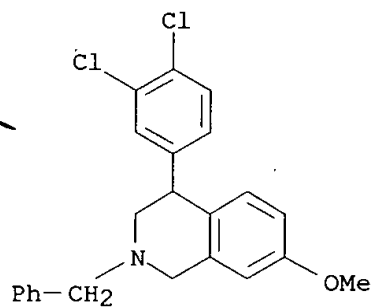
CN 7-Isoquinolinol, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-2-(1-methylethyl)-, hydrochloride (9CI) (CA INDEX NAME)





● HCl

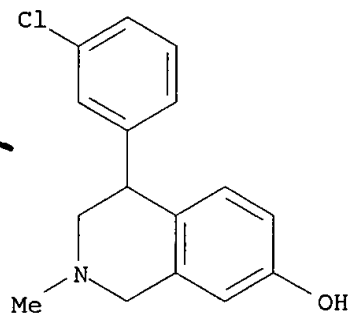
RN 34048-23-2 CAPLUS  
CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-(phenylmethyl)-, hydrochloride (9CI) (CA INDEX NAME)



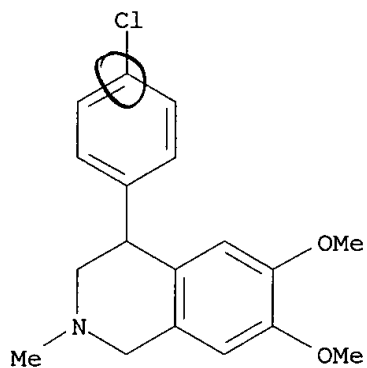
● HCl

RN 34154-25-1 CAPLUS  
CN 7-Isoquinolinol, 4-(3-chlorophenyl)-1,2,3,4-tetrahydro-2-methyl- (9CI)  
(CA INDEX NAME)

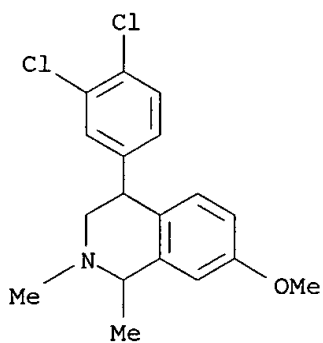
09/704,306



RN 34154-26-2 CAPLUS  
CN Isoquinoline, 4-(4-chlorophenyl)-1,2,3,4-tetrahydro-6,7-dimethoxy-2-methyl-  
(9CI) (CA INDEX NAME)



RN 43072-81-7 CAPLUS  
CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-1,2-  
dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

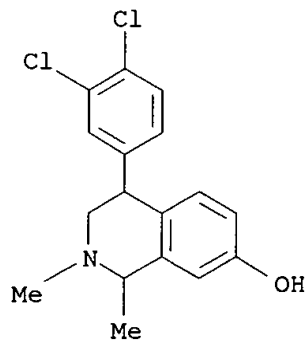
RN 43072-87-3 CAPLUS

Brenda Coleman

<page

09/704,306

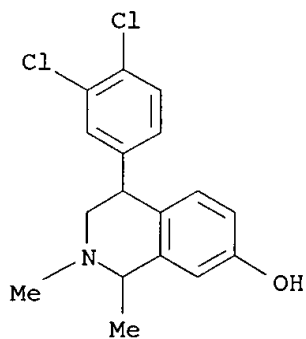
CN 7-Isoquinolinol, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-1,2-dimethyl-,  
hydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 43072-88-4 CAPLUS

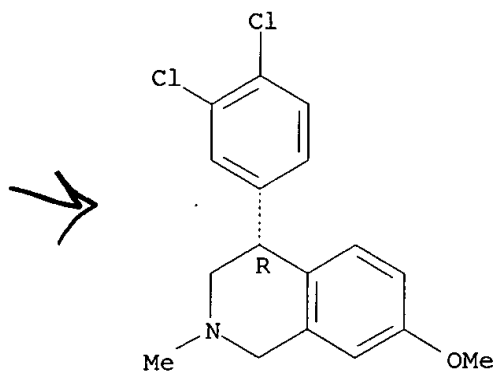
CN 7-Isoquinolinol, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-1,2-dimethyl-,  
(9CI) (CA INDEX NAME)



RN 43072-98-6 CAPLUS

CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-,  
hydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



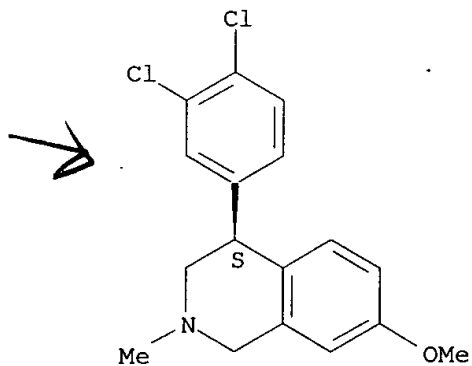
● HCl

RN 43073-00-3 CAPLUS  
 CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, [1R-(R\*,R\*)]-, compd.  
 with (S)-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-  
 methylisoquinoline (9CI) (CA INDEX NAME)

CM 1

CRN 50560-38-8  
 CMF C17 H17 Cl2 N O

Absolute stereochemistry.

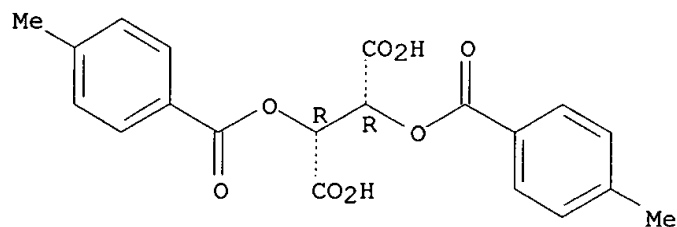


CM 2

CRN 32634-66-5  
 CMF C20 H18 O8

Absolute stereochemistry.

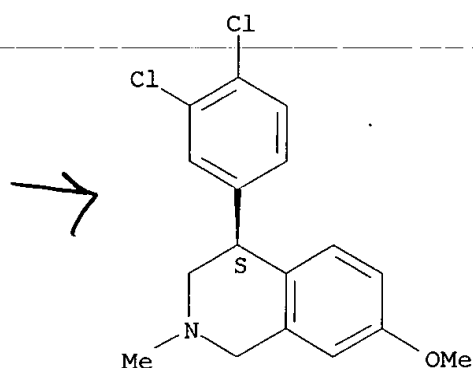
09/704,306



RN 43073-01-4 CAPLUS

CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-, hydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

RN 43170-70-3 CAPLUS

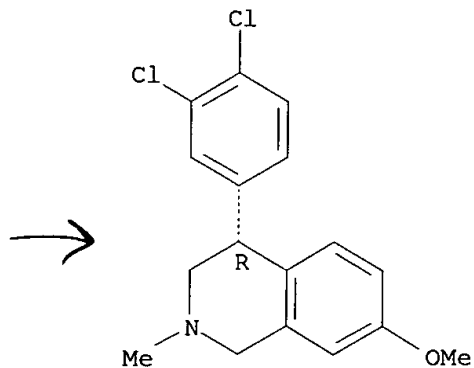
CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, [R-(R\*,R\*)]-, compd. with (R)-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methylisoquinoline (9CI) (CA INDEX NAME)

CM 1

CRN 50560-45-7

CMF C17 H17 Cl2 N O

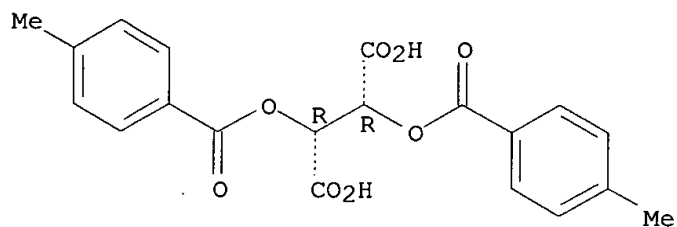
Absolute stereochemistry.



CM 2

CRN 32634-66-5  
CMF C20 H18 O8

Absolute stereochemistry.



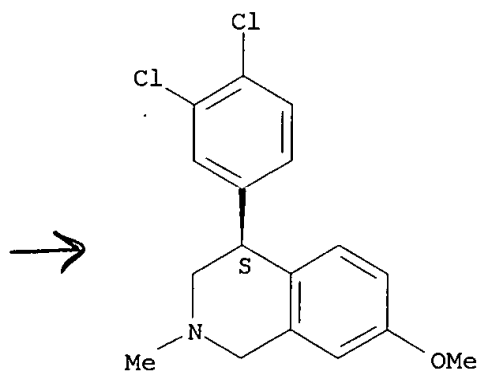
RN 43170-71-4 CAPLUS  
CN Butanedioic acid, 2,3-bis(benzoyloxy)-, [S-(R\*,R\*)]-, compd. with  
(S)-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-  
methylisoquinoline (9CI) (CA INDEX NAME)

CM 1

CRN 50560-38-8  
CMF C17 H17 Cl2 N O

Absolute stereochemistry.

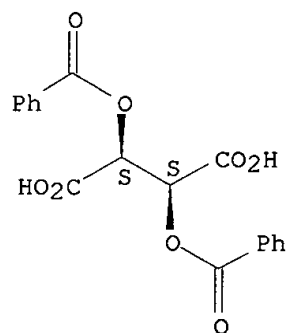
09/704,306



CM 2

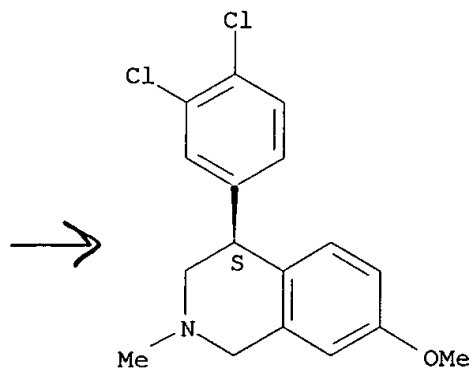
CRN 17026-42-5  
CMF C18 H14 O8

Absolute stereochemistry. Rotation (+).



RN 50560-38-8 CAPLUS  
CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



Brenda Coleman

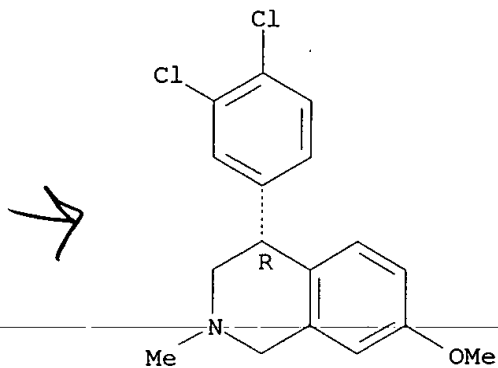
<page

09/704,306

RN 50560-45-7 CAPLUS

CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.





148 ANSWER 94 OF 100 CAPLUS COPYRIGHT 2003 ACS

AD 1973:427075 CAPLUS

DN 79:27075

TI 3,4-Dihydroisocarbostyrl and 1,2,3,4-tetrahydroisoquinoline derivatives of ephedrine

AU Trepanier, Donald L.; Sunder, Shyam

CS Hum. Health Res. Dev. Cent., Dow Chem. Co., Zionsville, IN, USA

SO Journal of Medicinal Chemistry (1973), 16(4), 342-7

CODEN: JMCMAR; ISSN: 0022-2623

DT Journal

LA English

AB Among 17 title compds. tested, 4-phenyl-2,3,8-trimethyl-1,2,3,4-tetrahydroisoquinoline (I) [40830-61-3] showed the best central nervous activity profile and behaved similarly to the antidepressants, imipramine and amitriptyline. I at 14.1 mg/kg i.p. in mice, antagonized reserpine-induced ptosis and HCl-induced writhing and potentiated d-amphetamine toxicity and hexobarbital sleep time. I was prepd. by reaction of l-ephedrine [299-42-3] with 2-methylbenzoyl chloride, redn. with B2H6 to form N-(2-methylbenzyl)ephedrine, and cyclization in the presence of concd. H2SO4.

IT 40830-61-3P 41958-50-3P 41958-51-4P

41958-58-1P 41958-59-2P

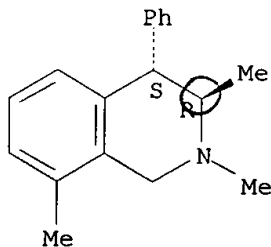
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(prepn. and central nervous system activity of)

RN 40830-61-3 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-2,3,8-trimethyl-4-phenyl-, trans- (9CI) (CA INDEX NAME)

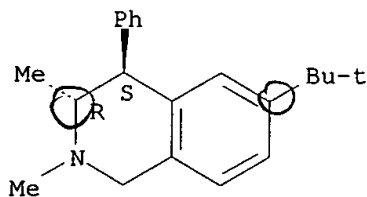
Relative stereochemistry.



RN 41958-50-3 CAPLUS

CN Isoquinoline, 6-(1,1-dimethylethyl)-1,2,3,4-tetrahydro-2,3-dimethyl-4-phenyl-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

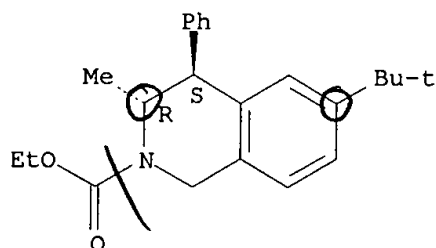


09/704,306

RN 41958-51-4 CAPLUS

CN 2(1H)-Isoquinolinecarboxylic acid, 6-(1,1-dimethylethyl)-3,4-dihydro-3-methyl-4-phenyl-, ethyl ester, trans- (9CI) (CA INDEX NAME)

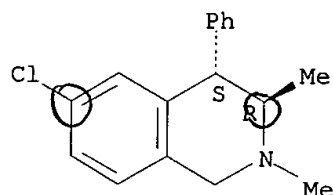
Relative stereochemistry.



RN 41958-58-1 CAPLUS

CN Isoquinoline, 6-chloro-1,2,3,4-tetrahydro-2,3-dimethyl-4-phenyl-, hydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

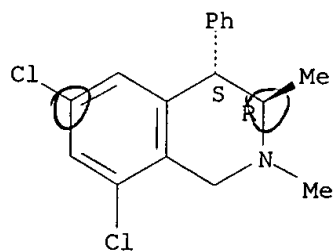


● HCl

RN 41958-59-2 CAPLUS

CN Isoquinoline, 6,8-dichloro-1,2,3,4-tetrahydro-2,3-dimethyl-4-phenyl-, hydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



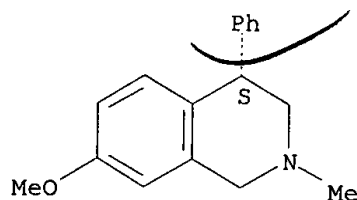
● HCl

09/704,306

198 ANSWER 95 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1972:475145 CAPLUS  
DN 77:75145  
TI 4-Phenylisoquinolines  
IN Grethe, Guenter; Uskokovic, Milan Radoje  
PA Hoffman-La Roche Inc.  
SO U.S., 10 pp.  
CODEN: USXXAM  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 3666763	A	19720530	US 1970-1062	19700106
PRAI	US 1970-1062		19700106		
GI	For diagram(s), see printed CA Issue.				
AB	4-Aryltetrahydroisoquinolines (I, R = H, Me, R1 = H, Me, PhCH2; R2 = Ph, p-MeC6H4; R3 = Cl, HO, MeO; R4 = H) useful as antidepressants and hypotensive agents were prepd. (chiefly as HCl salts) by reductive alkylation of di-hydroisoquinolones and hydrogenolysis of the tertiary OH groups. Some I were also resolved. Thus, 3 g Mg and 22 g PhBr in THF were treated with 25 g 2-benzyl-2,3,3-dihydro-7-methoxy-4(1H)-isoquinolone to give 32 g I.HCl (R = H, R1 = PhCH2, R2 = Ph, R3 = MeO, R4 = HO). Hydrogenation of 5.6 g I (R = H, R1 = PhCH2, R2 = Ph, R3 = MeO, R4 = HO) over Pd-C in HOAc at 60.degree. and 50 psi, followed by HCl-Me2-CHOH gave I.HCl (R = H, R1 = H, R2 = Ph, R3 = MeO, R4 = H). Alternately acid dehydration of the isoquinolinol with disproportionation of the dihydro product and metal hydride redn. of the isoquinoline gave I. I.HCl (R = H, Me; R1 = Me; R2 = Ph; R3 = MeO; R4 = H) had ED50 of 1.0 and 0.5 mg/kg resp. in the ptosis-anti-tetrabenazine test.				
IT	28102-56-9P 28102-57-0P 28102-58-1P 28102-59-2P 37617-41-7P 37617-51-9P 37617-55-3P 37617-56-4P 37624-18-3P 37624-22-9P 37624-24-1P 37624-25-2P 37624-26-3P 37624-27-4P 37624-28-5P 37624-29-6P 37757-49-6P RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)				
RN	28102-56-9 CAPLUS				
CN	Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-phenyl-, (S)- (8CI, 9CI) (CA INDEX NAME)				

Absolute stereochemistry.



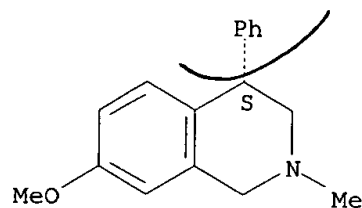
RN 28102-57-0 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-phenyl-, hydrochloride, (S)- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

Brenda Coleman

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09/704,306

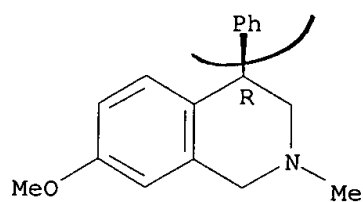


● HCl

RN 28102-58-1 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-phenyl-, (R)- (8CI, 9CI) (CA INDEX NAME)

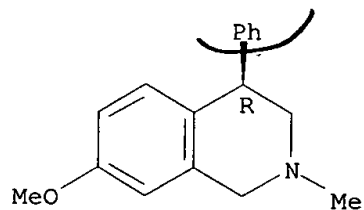
Absolute stereochemistry.

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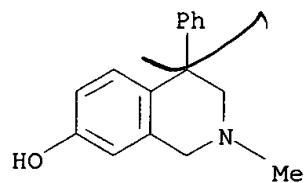
RN 28102-59-2 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-phenyl-, hydrochloride, (R)- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

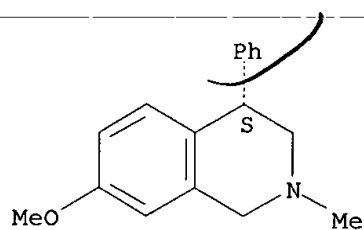
RN 37617-41-7 CAPLUS  
CN 7-Isoquinolinol, 1,2,3,4-tetrahydro-2-methyl-4-phenyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 37617-51-9 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-phenyl-, hydriodide, (S)- (9CI) (CA INDEX NAME)

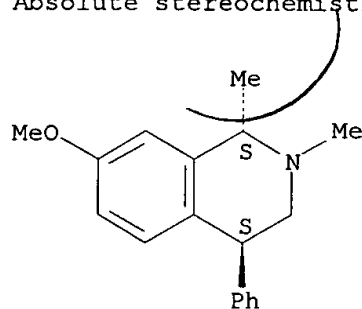
Absolute stereochemistry.



● HI

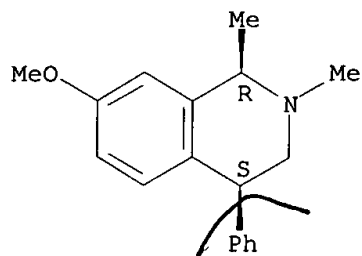
RN 37617-55-3 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-1,2-dimethyl-4-phenyl-, (1S-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



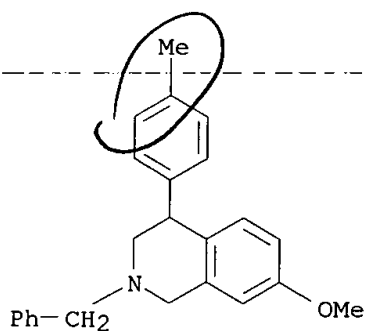
RN 37617-56-4 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-1,2-dimethyl-4-phenyl-, (1R-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 37624-18-3 CAPLUS

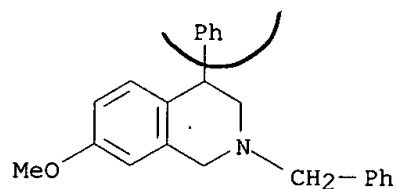
CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-4-(4-methylphenyl)-2-(phenylmethyl)-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 37624-22-9 CAPLUS

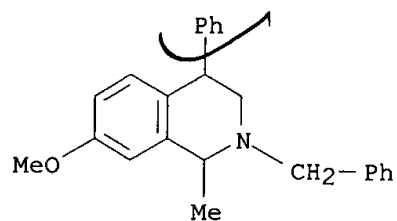
CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-4-phenyl-2-(phenylmethyl)-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 37624-24-1 CAPLUS

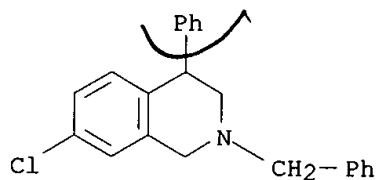
CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-1-methyl-4-phenyl-2-(phenylmethyl)-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

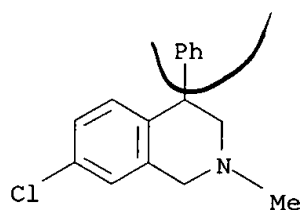
RN 37624-25-2 CAPLUS  
CN Isoquinoline, 7-chloro-1,2,3,4-tetrahydro-4-phenyl-2-(phenylmethyl)-, hydrochloride (9CI) (CA INDEX NAME)

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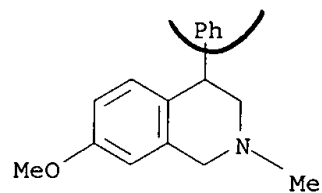
● HCl

RN 37624-26-3 CAPLUS  
CN Isoquinoline, 7-chloro-1,2,3,4-tetrahydro-2-methyl-4-phenyl-, hydrochloride (9CI) (CA INDEX NAME)



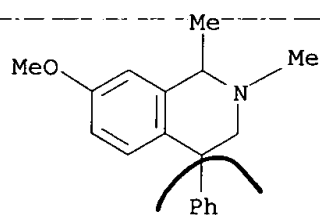
● HCl

RN 37624-27-4 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-phenyl-, hydrochloride (9CI) (CA INDEX NAME)



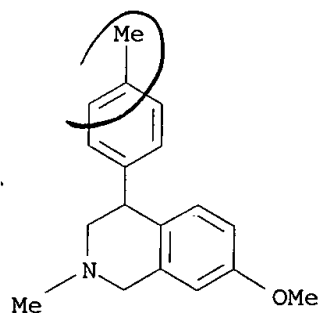
● HCl

RN 37624-28-5 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-1,2-dimethyl-4-phenyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

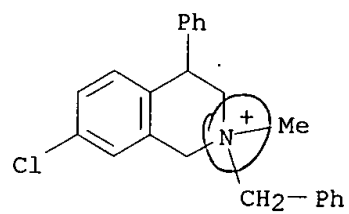
RN 37624-29-6 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-(4-methylphenyl)-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 37757-49-6 CAPLUS  
CN Isoquinolinium, 7-chloro-1,2,3,4-tetrahydro-2-methyl-4-phenyl-2-(phenylmethyl)-, iodide (9CI) (CA INDEX NAME)

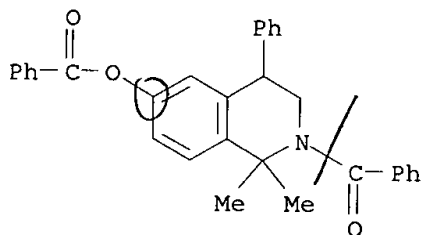




09/704,306

~~LA~~ 8 ANSWER 96 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1972:405364 CAPLUS  
DN 77:5364  
TI Tetrahydroisoquinolines  
IN Kegasawa, Kazuo; Hiiragi, Mineji; Ishimaru, Haruhide; Saito, Setsu;  
Kusama, Semeru  
PA Grelan Pharmaceutical Co., Ltd.  
SO Jpn. Tokkyo Koho, 15 pp.  
CODEN: JAXXAD  
DT **Patent**  
LA Japanese  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 47007381	B4	19720302	JP	19681230
GI	For diagram(s), see printed CA Issue.				
AB	The title compds. (I), analgesics, sedatives, and antiinflammatory agents, were manufd. from phenethylamines and carbonyl compds. E.g., 3-hydroxyphenethylamine and Me <sub>2</sub> CO in EtOH was refluxed 10 hr to give I (R <sub>1</sub> = R <sub>2</sub> = Me, R <sub>3</sub> = R <sub>4</sub> = R <sub>5</sub> = H). Similarly prepd. were 30 more I.				
IT	<b>36776-91-7P</b> RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)				
RN	36776-91-7 CAPLUS				
CN	6-Isoquinolinol, 2-benzoyl-1,2,3,4-tetrahydro-1,1-dimethyl-4-phenyl-, benzoate (ester) (9CI) (CA INDEX NAME)				



L48 ANSWER 97 OF 100 CAPLUS COPYRIGHT 2003 ACS  
 AN 1971:529683 CAPLUS  
 DN 75:129683  
 TI Antidepressive 1,2,3,4-tetrahydro-4-phenylisoquinoline derivatives  
 IN Rheiner, Alfred, Jr.  
 PA Hoffmann-La Roche, F., und Co., A.-G.  
 SO Ger. Offen., 58 pp.  
 CODEN: GWXXBX

DT Patent  
 LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2062001	A	19710715	DE 1970-2062001	19701216
	DE 2062001	C2	19861016		
	CH 527194	A	19720831	CH 1970-527194	19700106
	SE 368401	B	19740701	SE 1970-17063	19701216
	SE 386672	B	19760816	SE 1973-13623	19701216
	ZA 7008590	A	19710929	ZA 1970-8590	19701221
	IL 35916	A1	19731128	IL 1970-35916	19701228
	NL 7018956	A	19710708	NL 1970-18956	19701229
	NL 171444	B	19821101		
	NL 171444	C	19830405		
	FI 49503	B	19750401	FI 1970-3519	19701231
	BE 761219	A1	19710705	BE 1971-98281	19710105
	FR 2081412	A5	19711203	FR 1971-97	19710105
	FR 2081412	B1	19740412		
	AT 303041	B	19721110	AT 1971-45	19710105
	DK 125021	B	19721218	DK 1971-25	19710105
	GB 1335261	A	19731024	GB 1971-454	19710105
	ES 387016	A1	19760501	ES 1971-387016	19710105
	NO 135315	B	19761213	NO 1971-21	19710105
	CA 999866	A1	19761116	CA 1971-102060	19710106
	JP 55015476	B4	19800423	JP 1971-94	19710106
-US	3947456	A	19760330	US 1973-365921	19730601
NO	135062	B	19761025	NO 1974-554	19740219
NO	135314	B	19761213	NO 1974-555	19740219
PRAI	CH 1970-103		19700106		
	US 1970-102551		19701229		
	NO 1971-21		19710105		

GI For diagram(s), see printed CA Issue.

AB The title compds. (I) were prepd. by reductive cyclization. Thus, .alpha.-(aminomethyl)-4-chlorobenzyl alc.-HCl and m-MeOC<sub>6</sub>H<sub>4</sub>CHO were reduced with NaBH<sub>4</sub> and the product cyclized with dil. aq. H<sub>2</sub>SO<sub>4</sub> to give I (R = MeO, R<sub>1</sub> = R<sub>2</sub> = R<sub>3</sub> = H, R<sub>4</sub> = Cl). Among compds. prepd. were I (R<sub>1</sub> = R<sub>2</sub> = H, R<sub>3</sub> = Me) (R and R<sub>4</sub> given): OH, Cl or Cl<sub>2</sub>; MeO, Cl or Cl<sub>2</sub>.

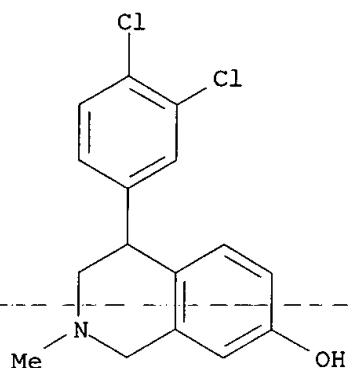
IT 34041-51-5P 34041-52-6P 34041-53-7P  
 34041-54-8P 34041-59-3P 34041-60-6P  
 34041-61-7P 34041-65-1P 34041-66-2P  
 34041-67-3P 34041-70-8P 34041-71-9P  
 34041-72-0P 34041-73-1P 34041-77-5P  
 34041-78-6P 34041-83-3P 34041-84-4P  
 34047-49-9P 34047-53-5P 34047-54-6P  
 34047-58-0P 34047-59-1P 34047-60-4P  
 34048-10-7P 34048-11-8P 34048-12-9P  
 34048-13-0P 34048-14-1P 34048-18-5P  
 34048-19-6P 34048-20-9P 34048-21-0P  
 34048-22-1P 34048-23-2P 34153-05-4P

**34154-25-1P 34154-26-2P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 34041-51-5 CAPLUS

CN 7-Isoquinolinol, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-2-methyl-,  
hydrobromide (8CI, 9CI) (CA INDEX NAME)

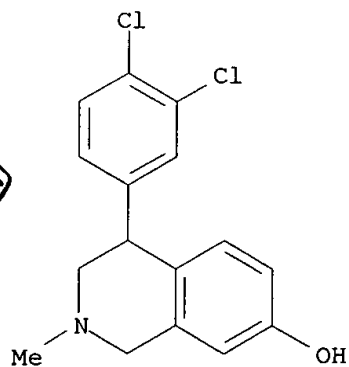


E

● HBr

RN 34041-52-6 CAPLUS

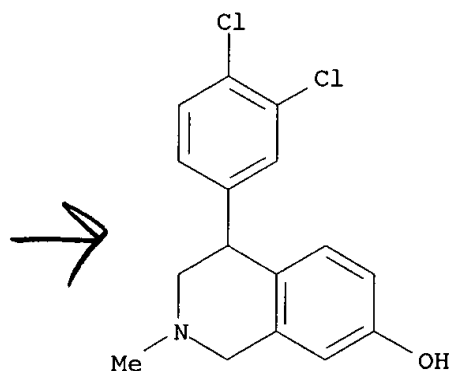
CN 7-Isoquinolinol, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-2-methyl- (8CI,  
9CI) (CA INDEX NAME)



E

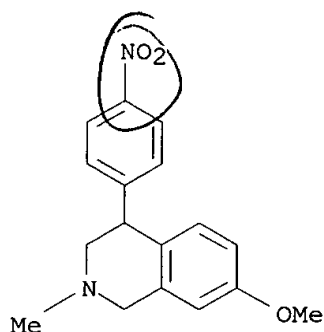
RN 34041-53-7 CAPLUS

CN 7-Isoquinolinol, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-2-methyl-,  
hydrochloride (8CI, 9CI) (CA INDEX NAME)



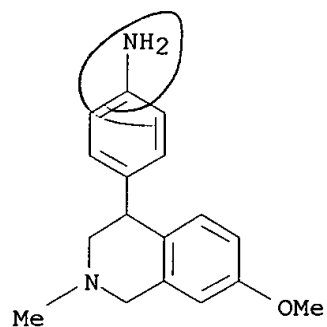
● HCl

RN 34041-54-8 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-(4-nitrophenyl)-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

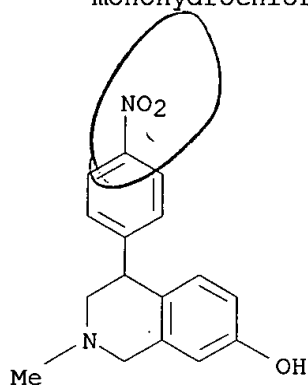
RN 34041-59-3 CAPLUS  
CN Benzenamine, 4-(1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-isoquinolinyl)-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

RN 34041-60-6 CAPLUS

CN 7-Isoquinolinol, 1,2,3,4-tetrahydro-2-methyl-4-(4-nitrophenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

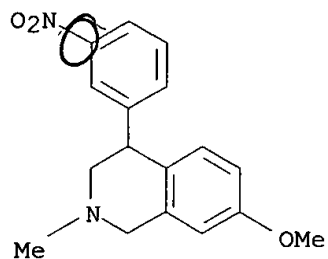


● HCl

RN 34041-61-7 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-(3-nitrophenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

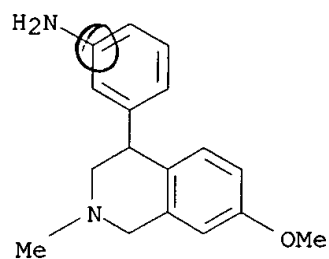
09/704,306



● HCl

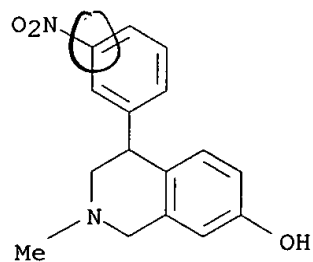
RN 34041-65-1 CAPLUS  
CN Benzenamine, 3-(1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-isoquinolinyl)-,  
dihydrochloride (9CI) (CA INDEX NAME)

---



●2 HCl

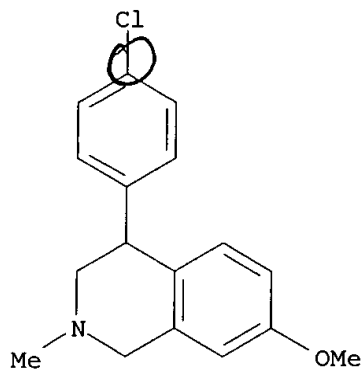
RN 34041-66-2 CAPLUS  
CN 7-Isoquinolinol, 1,2,3,4-tetrahydro-2-methyl-4-(3-nitrophenyl)-,  
hydrochloride (9CI) (CA INDEX NAME)



● HCl

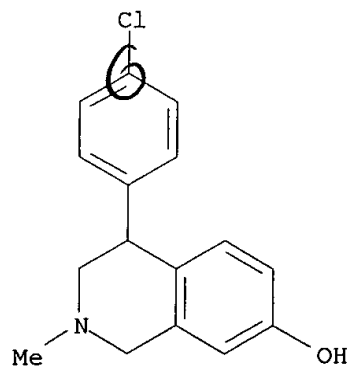
RN 34041-67-3 CAPLUS  
CN Isoquinoline, 4-(4-chlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-,  
dihydrochloride (9CI) (CA INDEX NAME)

hydrochloride (9CI) (CA INDEX NAME)



● HCl

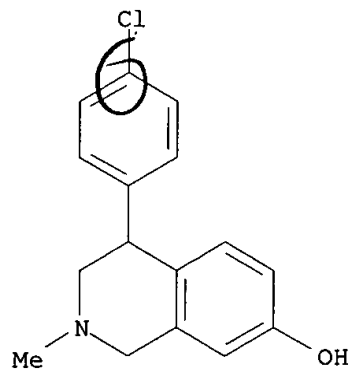
RN 34041-70-8 CAPLUS  
CN 7-Isoquinolinol, 4-(4-chlorophenyl)-1,2,3,4-tetrahydro-2-methyl-,  
hydrobromide (9CI) (CA INDEX NAME)



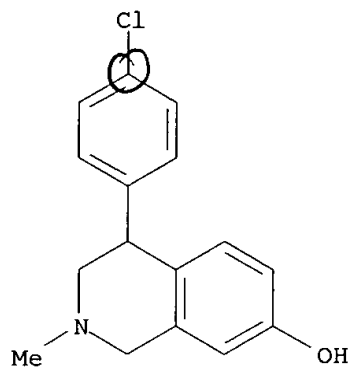
● HBr

RN 34041-71-9 CAPLUS  
CN 7-Isoquinolinol, 4-(4-chlorophenyl)-1,2,3,4-tetrahydro-2-methyl- (9CI)  
(CA INDEX NAME)





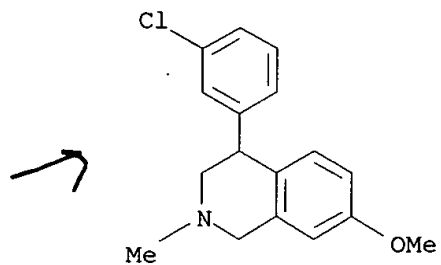
RN 34041-72-0 CAPLUS  
CN 7-Isoquinolinol, 4-(p-chlorophenyl)-1,2,3,4-tetrahydro-2-methyl-,  
hydrochloride, (.+-.)- (8CI) (CA INDEX NAME)



● HCl

RN 34041-73-1 CAPLUS  
CN Isoquinoline, 4-(3-chlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-,  
hydrochloride (9CI) (CA INDEX NAME)

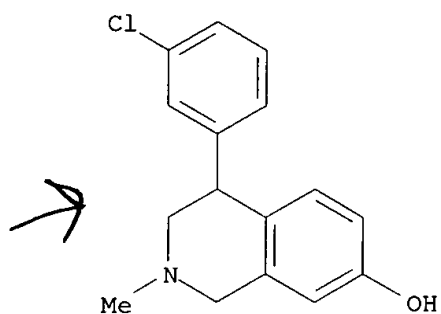
09/704,306



E

● HCl

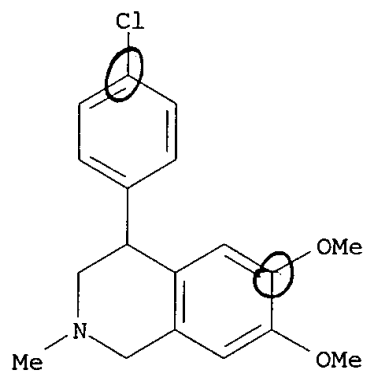
RN 34041-77-5 CAPLUS  
CN 7-Isoquinolinol, 4-(3-chlorophenyl)-1,2,3,4-tetrahydro-2-methyl-,  
hydrochloride (9CI) (CA INDEX NAME)



E

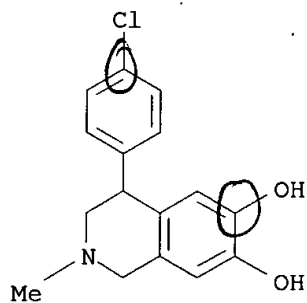
● HCl

RN 34041-78-6 CAPLUS  
CN Isoquinoline, 4-(4-chlorophenyl)-1,2,3,4-tetrahydro-6,7-dimethoxy-2-methyl-,  
hydrochloride (9CI) (CA INDEX NAME)



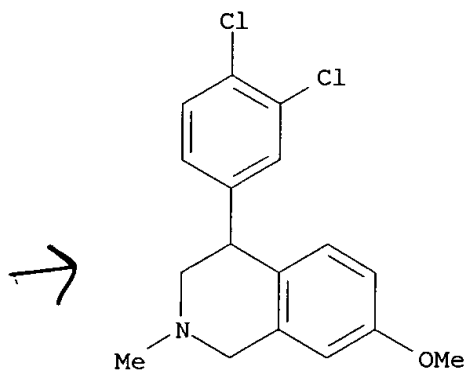
● HCl

RN 34041-83-3 CAPLUS  
CN 6,7-Isoquinolinediol, 4-(4-chlorophenyl)-1,2,3,4-tetrahydro-2-methyl-, hydrobromide (9CI) (CA INDEX NAME)



● HBr

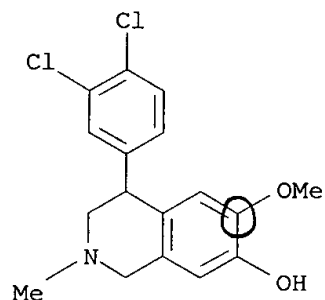
RN 34041-84-4 CAPLUS  
CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-methyl-, hydrochloride (8CI, 9CI) (CA INDEX NAME)



E

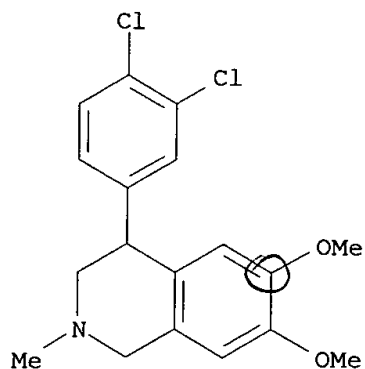
● HCl

RN 34047-49-9 CAPLUS  
 CN 7-Isoquinolinol, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-6-methoxy-2-methyl-, hydrochloride (8CI, 9CI) (CA INDEX NAME)



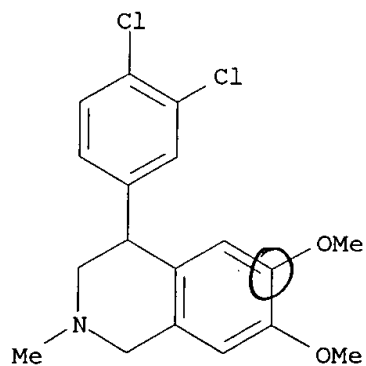
● HCl

RN 34047-53-5 CAPLUS  
 CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-6,7-dimethoxy-2-methyl-, hydrochloride (8CI, 9CI) (CA INDEX NAME)



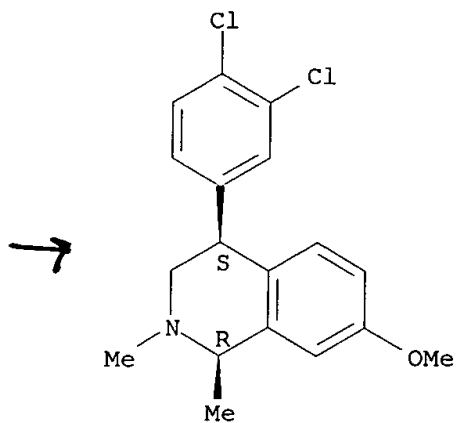
● HCl

RN 34047-54-6 CAPLUS  
CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-6,7-dimethoxy-2-methyl- (8CI, 9CI) (CA INDEX NAME)



RN 34047-58-0 CAPLUS  
CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-1,2-dimethyl-, hydrochloride, cis-(.+-.)- (8CI) (CA INDEX NAME)

Relative stereochemistry.

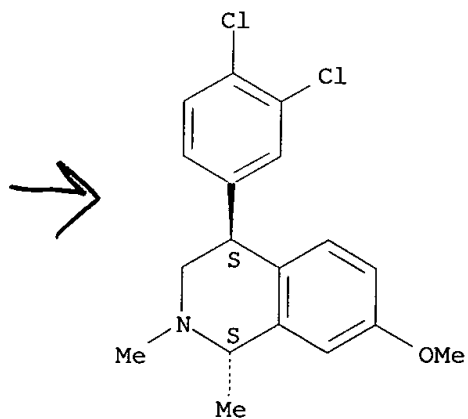


E

● HCl

RN 34047-59-1 CAPLUS  
 CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-1,2-dimethyl-, hydrochloride, trans-(+)- (8CI) (CA INDEX NAME)

Relative stereochemistry.



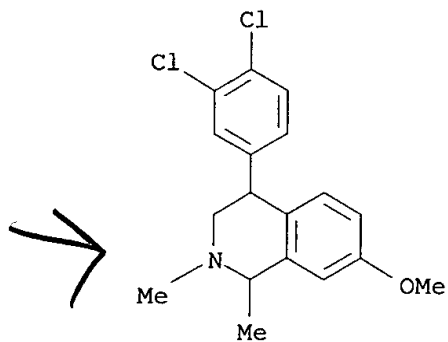
E

● HCl

RN 34047-60-4 CAPLUS  
 CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-1,2-dimethyl-, 2-hydroxy-1,2,3-propanetricarboxylate (9CI) (CA INDEX NAME)

CM 1

CRN 47205-36-7  
 CMF C18 H19 Cl2 N O

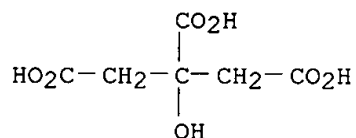


CM 2

E

CRN 77-92-9

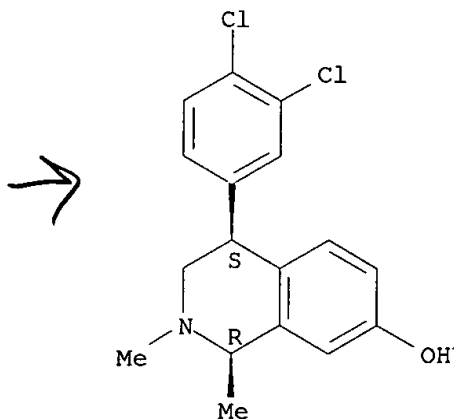
CMF C6 H8 O7



RN 34048-10-7 CAPLUS

CN 7-Isoquinolinol, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-1,2-dimethyl-,  
cis-(.+-.)- (8CI) (CA INDEX NAME)

Relative stereochemistry.

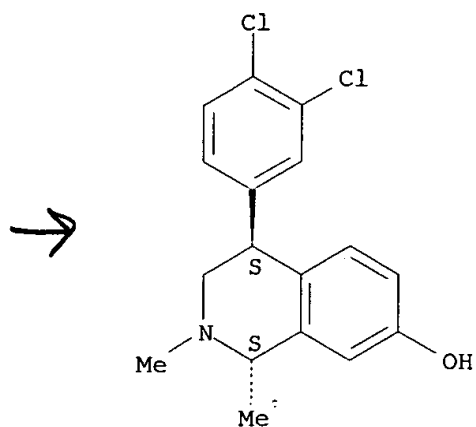


E

RN 34048-11-8 CAPLUS

CN 7-Isoquinolinol, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-1,2-dimethyl-,  
hydrochloride, trans-(.+-.)- (8CI) (CA INDEX NAME)

Relative stereochemistry.

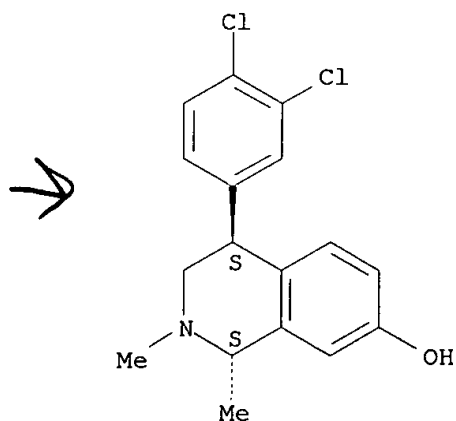


E

● HCl

RN 34048-12-9 CAPLUS  
CN 7-Isoquinolinol, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-1,2-dimethyl-, trans-(.+-.)- (8CI) (CA INDEX NAME)

Relative stereochemistry.

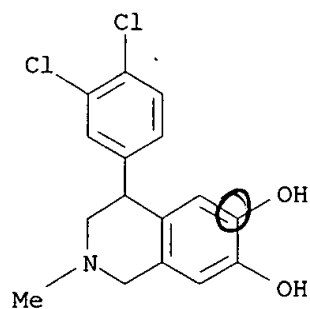


E

RN 34048-13-0 CAPLUS  
CN 6,7-Isoquinolinediol, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-2-methyl-, hydrobromide (8CI, 9CI) (CA INDEX NAME)

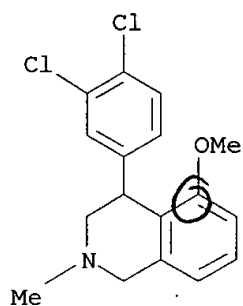


09/704,306



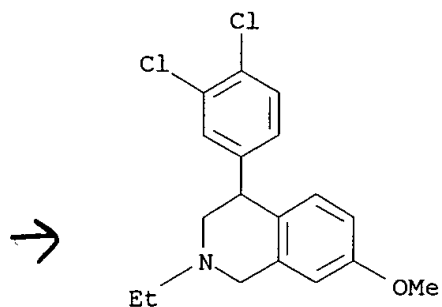
● HBr

RN 34048-14-1 CAPLUS  
CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-5-methoxy-2-methyl-, hydrochloride, (+-)- (8CI) (CA INDEX NAME)



● HCl

RN 34048-18-5 CAPLUS  
CN Isoquinoline, 4-(3,4-dichlorophenyl)-2-ethyl-1,2,3,4-tetrahydro-7-methoxy-, hydrochloride (8CI, 9CI) (CA INDEX NAME)

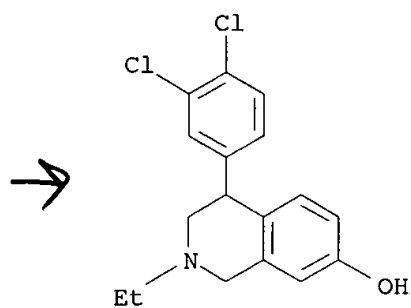


E

● HCl

RN 34048-19-6 CAPLUS

CN 7-Isoquinolinol, 4-(3,4-dichlorophenyl)-2-ethyl-1,2,3,4-tetrahydro-, hydrochloride (8CI, 9CI) (CA INDEX NAME)

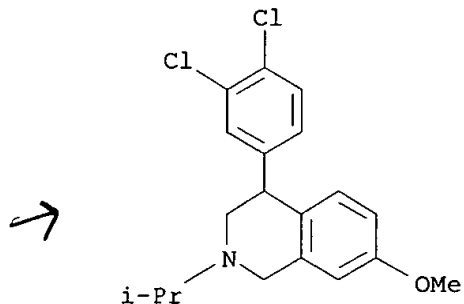


E

● HCl

RN 34048-20-9 CAPLUS

CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-(1-methylethyl)-, hydrochloride (9CI) (CA INDEX NAME)

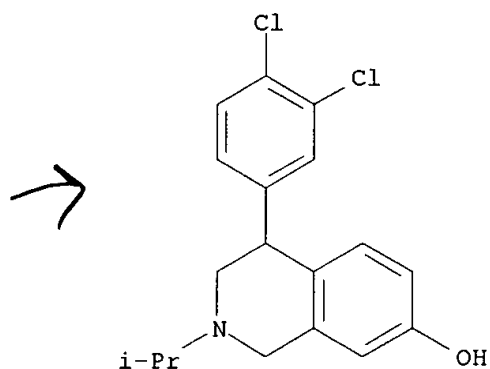


E

● HCl

RN 34048-21-0 CAPLUS

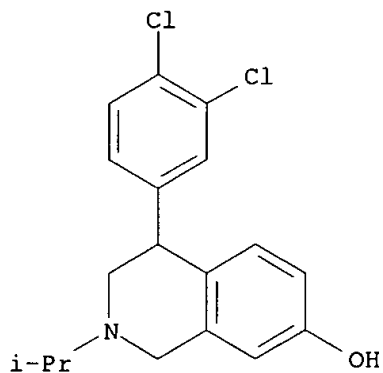
CN 7-Isoquinolinol, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-2-(1-methylethyl)- (9CI) (CA INDEX NAME)



E

RN 34048-22-1 CAPLUS

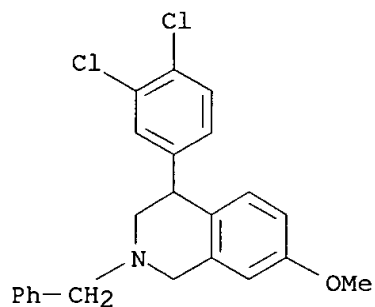
CN 7-Isoquinolinol, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-2-(1-methylethyl)-, hydrochloride (9CI) (CA INDEX NAME)



E

● HCl

RN 34048-23-2 CAPLUS  
 CN Isoquinoline, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-7-methoxy-2-(phenylmethyl)-, hydrochloride (9CI) (CA INDEX NAME)

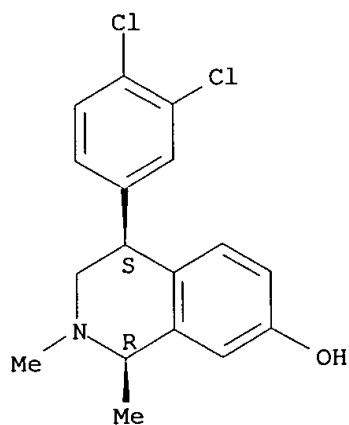


E

● HCl

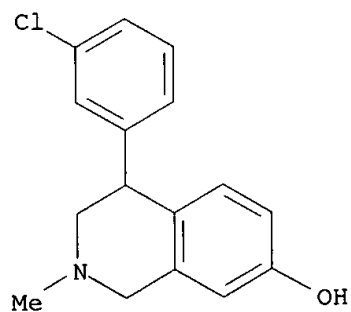
RN 34153-05-4 CAPLUS  
 CN 7-Isoquinolinol, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-1,2-dimethyl-, hydrochloride, cis-(.+-.)- (8CI) (CA INDEX NAME)

Relative stereochemistry.

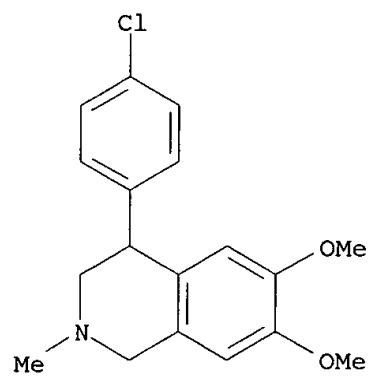


● HCl

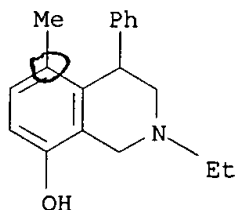
RN 34154-25-1 CAPLUS  
CN 7-Isoquinolinol, 4-(3-chlorophenyl)-1,2,3,4-tetrahydro-2-methyl- (9CI)  
(CA INDEX NAME)



RN 34154-26-2 CAPLUS  
CN Isoquinoline, 4-(4-chlorophenyl)-1,2,3,4-tetrahydro-6,7-dimethoxy-2-methyl-  
(9CI) (CA INDEX NAME)



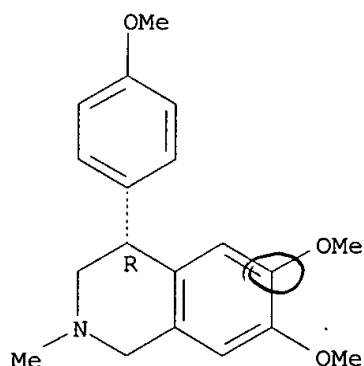
148 ANSWER 98 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1971:420364 CAPLUS  
DN 75:20364  
TI Acid-catalyzed rearrangements of 2,3-dihydro-2-phenyl-1,4-benzoxazepin-5(4H)-ones  
AU Misiti, Domenico  
CS Dep. Ther. Chem., Ist. Super. Sanita, Italy  
SO Annali dell'Istituto Superiore di Sanita (1970), 6(Pt. 4-5), 318-19  
CODEN: AISSAW; ISSN: 0021-2571  
DT Journal  
LA English  
GI For diagram(s), see printed CA Issue.  
AB The title compd. (I, R = H) treated with H<sub>2</sub>SO<sub>4</sub> or polyphosphoric acids was readily converted into the 2 isomeric compds. II (R = H) and III (R = H) in the ratio of 10:1 by protonation of the ether O and formation of the more stable carbonium ion. The latter rearranged to give mainly II (R = H) together with a small amt. of III (R = H), formed by a Friedel-Crafts type electrophilic attack on the aromatic nucleus. This attack should be facilitated by an electron-releasing substituent on the aromatic nucleus of the initial benzoxazepinone. I (R = Me) treated as above gave the isomeric II (R = Me) and III (R = Me) in the inverse ratio of 1:10, showing enhancement of the Friedel-Crafts condensation of the presence of the Me group.  
IT **33191-23-0P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)  
RN 33191-23-0 CAPLUS  
CN 8-Isoquinolinol, 2-ethyl-1,2,3,4-tetrahydro-5-methyl-4-phenyl- (8CI) (CA INDEX NAME)



09/704,306

~~128~~ ANSWER 99 OF 100 CAPLUS COPYRIGHT 2003 ACS  
AN 1970:78138 CAPLUS  
DN 72:78138  
TI Determination of the absolute configuration of 4-phenyl-1,2,3,4-tetrahydroisoquinolines utilizing ORD and CD spectroscopy  
AU Toome, V.; Blount, J. F.; Grethe, G.; Uskokovic, M.  
CS Chem. Res. Div., Hoffmann-La Roche Inc., Nutley, NJ, USA  
SO Tetrahedron Letters (1970), (1), 49-52  
CODEN: TELEAY; ISSN: 0040-4039  
DT Journal  
LA English  
GI For diagram(s), see printed CA Issue.  
AB The C-4 configuration of a no. of I free bases (A) or HCl salts(B) was detd. by ORD and CD spectroscopy. The following compds. were prepd. (R, R1, R2, R3, free base or salt, configuration and [.alpha.]D, given): Me, H, H, H, A, S, 18.4.degree.; Me, H, H, H, B, S, 1.9.degree.; Me, H, H, H, B, R, -2.2.degree.; H, H, OMe, H, A, S, -9.8.degree.; H, H, OMe, H, A, R, 10.1.degree.; Me, H, OMe, H, A, S, 7.2; Me, H, OMe, H, B, S, -11.8.degree.; Me, H, OMe, H, A, R, -7.1.degree.; Me, H, OMe, H, B, R, 11.5.degree.; H, OMe, OMe, OMe, A, S, -38.2.degree.; H, OMe, OMe, OMe, A, R, 38.4.degree.; Me, OMe, OMe, OMe, A, S, -21.7.degree.; Me, OMe, OMe, OMe, A, R, 21.6.degree.; 4-BrC6H4CO, OMe, OMe, OMe, A, S, 120.degree.. The last compd. was studied by x-ray crystallography. The monoclinic crystals showed the space group P21 and the lattice parameters a 15.704, b 5.902, and c 12.969 .ANG., .beta. 110.59.degree. and Z 2.  
IT 23330-76-9 23330-78-1 23367-60-4  
28102-56-9 28102-57-0 28102-58-1  
28102-59-2  
RL: PRP (Properties)  
(configuration of)  
RN 23330-76-9 CAPLUS  
CN Isoquinoline, 1,2,3,4-tetrahydro-6,7-dimethoxy-4-(4-methoxyphenyl)-2-methyl-, (R)- (9CI) (CA INDEX NAME)

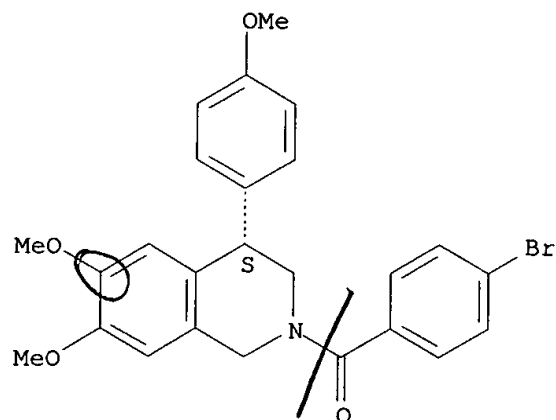
Absolute stereochemistry.



RN 23330-78-1 CAPLUS  
CN Cherylline, 2-(p-bromobenzoyl)-2-demethyl-O,O-dimethyl- (8CI) (CA INDEX NAME)

Absolute stereochemistry.

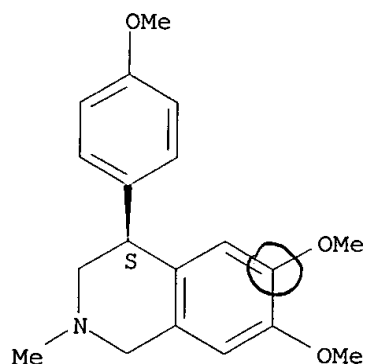




RN 23367-60-4 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-6,7-dimethoxy-4-(4-methoxyphenyl)-2-methyl-, (S)- (9CI) (CA INDEX NAME)

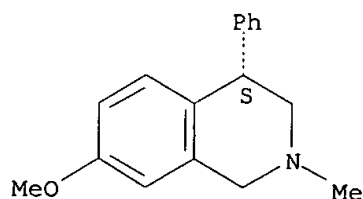
Absolute stereochemistry. Rotation (-).



RN 28102-56-9 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-phenyl-, (S)- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

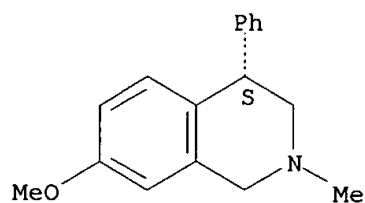


RN 28102-57-0 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-phenyl-, hydrochloride, (S)- (8CI, 9CI) (CA INDEX NAME)

09/704,306

Absolute stereochemistry.

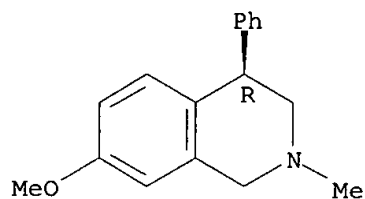


● HCl

RN 28102-58-1 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-phenyl-, (R)- (8CI, 9CI) (CA INDEX NAME)

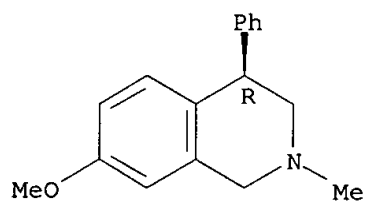
Absolute stereochemistry.



RN 28102-59-2 CAPLUS

CN Isoquinoline, 1,2,3,4-tetrahydro-7-methoxy-2-methyl-4-phenyl-, hydrochloride, (R)- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

~~148~~ ANSWER 100 OF 100 CAPLUS COPYRIGHT 2003 ACS  
~~AN~~ 1959:89584 CAPLUS  
 DN 53:89584  
 OREF 53:16180a-i,16181a-f  
 TI Pavine. III. Related syntheses  
 AU Battersby, A. R.; Binks, R.  
 CS Univ. Bristol, UK  
 SO J. Chem. Soc. (1958) 4333-9  
 DT Journal  
 LA Unavailable  
 AB cf. C.A. 2, 17311i. N-Acetyl-1,2-bis(3,4-dimethoxyphenyl)ethylamine, 3,4  
 - (MeO)2C6H3CH2CHRC6H3(OMe)2-3,4 (I, R = NHAc) (II), treated with P2O5 in  
 boiling PhMe gave a dimer (III) of [3,4-(MeO)2C6H3CH:]2 (IV) instead of  
 the expected 1-methyl-6,7-dimethoxy-3-(3,4-dimethoxyphenyl)-3,4-  
 dihydroisoquinoline (V). (I, R = NH2) (VI) treated with HCHO and HCO2H  
 gave a 1,2,3,4-tetrahydroisoquinoline (VII) and VI treated with AcH and  
 H2SO4 yielded the corresponding 1-methyl-1,2,3,4-tetrahydroisoquinoline  
 (VIII), dehydrogenated in good yield with Hg(OAc)2 to V. HCO2NH4 (50 g.),  
 10 ml. 90% HCO2H, and 25 g. 3,4-(MeO)2C6H3CH2COC6H3(OMe)2-3,4 (IX) heated  
 at 150-80.degree. at a rate moderated to prevent foaming, kept 3 hrs. at  
 185.degree., the cooled product taken up in 200 ml. H2O and 1 l. C6H6, the  
 C6H6 layer evapd., the residue refluxed 1.25 hrs. in 150 ml. 5N H2SO4, the  
 cooled soln. extd. 3 times with 200 ml. Et2O, the aq. layer made strongly  
 alk., and the ppt. crystd. (H2O) yielded 63% VI, m. 107.degree.; II m.  
 161-2.degree. (cf. Allen and Buck, C.A. 24, 1115). II (0.8 g.) in dry  
 boiling PhMe treated with 2 g. dry Filtercel and 2 g. P2O5, 2 g. P2O5  
 added after 15 min. and again after 30 min., the mixt. boiled 30 min.  
 longer, the cooled suspension poured onto ice, the mixt. filtered, the  
 residue washed with hot PhMe, the org. layer washed with excess dil. HCl,  
 the combined aq. layer and washings extd. 3 times with EtOAc, and the  
 combined aq. layer and washings extd. 3 times with EtOAc, and the combined  
 dried org. solns. evapd. gave 0.579 g. neutral fraction, crystd. (alc.) to  
 yield 0.244 g. III, m. 155-6.degree.. The extd. aq. layer made strongly  
 alk. with KOH and extd. 3 times with Et2O produced 31 mg. gum. VI (1 g.)  
 and 0.5 g. anhyd. Na2CO3 in 30 ml. H2O and 45 ml. purified dioxane  
 refluxed 10 hrs. with 6 ml. MeI, the cooled soln. treated with aq.  
 Na2S2O3, the iodine-free soln. evapd. to eliminate dioxane and unchanged  
 MeI, and the suspension extd. 3 times with 10:1 Et2O-CHCl3 gave 0.1 g.  
 solid [recrystd. (alc.) to yield 30 mg. needles, m. 117-18.degree.]. The  
 aq. alk. layer acidified, treated with 10 g. KI, extd. 3 times with CHCl3,  
 the dried ext. evapd. at 40.degree., and the cryst. residue recrystd.  
 (alc.) gave 1.38 g. VI.MeI (X), m. 179-80.degree. (decompn.). X (0.8 g.)  
 in 40 ml. warm H2O shaken 30 min. with moist Ag2O (from 2 g. AgNO3), the  
 filtered soln. and 60 ml. washings refluxed 2 hrs. with 80 g. NaOH, the  
 cooled soln. extd. 3 times with Et2O, and the product crystd. (alc.)  
 yielded 92% IV, m. 153-4.degree., hydrogenated in alc. with PtO2 at  
 17.degree./751 mm. to give [3,4-(MeO)2C6H3CH2]2, m. 108-9.degree.. IX (1  
 g.) in 150 ml. alc. shaken 5 hrs. at 20.degree./758 mm. with H and 10%  
 Pd-C, the filtered soln. evapd., part (0.3 g.) of the cryst. residue  
 refluxed 7 hrs. with 15 ml. aq. 2N H2SO4, the soln. cooled, and the cryst.  
 product recrystd. (alc.) gave IV, .lambda. 303 m.mu. (log .epsilon. 4.14,  
 alc.). IV (0.2 g.) refluxed 8 hrs. in 20 ml. dry PhMe with 2 g. P2O5  
 (exposed to air 1 min.) and the mixt. worked up gave 50 mg. III, m.  
 153-6.degree. (alc.). VI (1 g.) heated 8 hrs. at 100.degree. with 5 ml.  
 95% HCO2H and 5 ml. 37% HCHO, the soln. poured into H2O, and the mixt.  
 basified and extd. with 10:1 Et2O-CHCl3 gave 0.92 g. VII,  
 6,7-dimethoxy-3-(3,4-dimethoxyphenyl)-2-methyl-1,2,3,4-  
 tetrahydroisoquinoline, m. 123-5.degree. (30% alc.); MeI deriv. (XI) m.

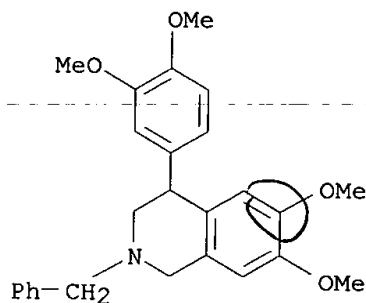
250-2.degree. (decompn.). XI (0.412 g.) refluxed 5 hrs. with 0.5 g. AgNO<sub>3</sub> and 20 g. KOH in 30 ml. H<sub>2</sub>O, the products sepd. into 16 mg. neutral and 240 mg. basic fraction, and recrystd. (dil. alc.) gave 0.17 g. 2-dimethylaminomethyl-3',4,4',5-tetramethoxystilbene, m. 101-3.degree.,  $\lambda$ . 289 m. $\mu$ . (log  $\epsilon$ . 4.12, alc.), hydrogenated in alc. at 18.degree./743 min. over PtO<sub>2</sub> with uptake of 1 mole H in 2 hrs. VI (3 g.) in 120 ml. 6N H<sub>2</sub>SO<sub>4</sub> refluxed 1 hr. with 9 ml. AcH, the cooled soln. kept overnight with 9 ml. AcOH, the mixt. refluxed 5 hrs. with 6 ml. AcH, and the soln. extd. with Et<sub>2</sub>O gave 0.28 g. IV, m. 151-2.degree. (alc.). The main aq. soln. strongly basified with KOH and extd. 3 times with Et<sub>2</sub>O yielded 74% VIII, 6,7-dimethoxy-3-(3,4-dimethoxyphenyl)-1-methyl-1,2,3,4-tetrahydroisoquinoline, m. 130-3.degree. (dil. alc.),  $\lambda$ . 229,281 m. $\mu$ . (log  $\epsilon$ . 4.2, 3-82, alc.); N-Ac deriv., resin. VIII (2.2 g.) in 35 ml. H<sub>2</sub>O and 3-5 ml. AcOH warmed gently with 10 g. Hg(OAc)<sub>2</sub>, the clear soln. refluxed 9 hrs., the cooled soln. filtered, the residue washed with H<sub>2</sub>O and alc., the filtrate and washings satd. 10 min. at 55.degree. with H<sub>2</sub>S, the soln. acidified with 25 ml. 2N HCl, and satd. 1 hr. with H<sub>2</sub>S gave a ppt. This was coagulated by heating, the mixt. filtered, the residue washed 3 times with 30 ml. acidified hot H<sub>2</sub>O (contg. a few drops of 2N HCl) and 3 times with 30 ml. acidified boiling alc., the combined filtrate and washings freed from alc., washed 3 times with Et<sub>2</sub>O, the aq. layer made strongly alk. with KOH, extd. 3 times with 100 ml. Et<sub>2</sub>O, the cryst. basic product (1.85 g.) taken up in alc., treated with 1.5 g. (CO<sub>2</sub>H)<sub>2</sub>.2H<sub>2</sub>O in a min. of H<sub>2</sub>O, the ppt. crystd. (1.2 l. alc.), and the product (2.02 g., m. 217.degree.) recrystd. (alc.) gave V oxalate, m. 219.degree. (decompn.),  $\lambda$ . 241, 303, 352 m. $\mu$ . (log  $\epsilon$ . 4.33, 3.93, 3.83, alc.). V oxalate converted by treatment with aq. alkali and extn. with Et<sub>2</sub>O gave V, m. 115-16.degree. (dil. alc.),  $\lambda$ . 231, 278, 310 m. $\mu$ . (log  $\epsilon$ . 4.58, 4.04, 3.85, alc.). V (23.6 mg.) hydrogenated 12 min. in 5 ml. alc. with 10 mg. PtO<sub>2</sub> at 19.degree./747 mm. and the filtered soln. evapd. gave VIII. VIII (0.2 g.) heated 15 hrs. at 100-10.degree. in 4 ml. 95% HCO<sub>2</sub>H and 8 ml. 37% HCHO, the mixt. poured into 20 ml. 0.1N HCl, extd. 3 times with Et<sub>2</sub>O, the aq. soln. made alk. with NaOH, extd. 3 times with Et<sub>2</sub>O, and the gummy product converted with HClO<sub>4</sub> gave 0.25 g. 6,7-dimethoxy-3-(3,4-dimethoxyphenyl)-1,2-dimethyl-1,2,3,4-tetrahydroisoquinoline (XII).HClO<sub>4</sub>, m. 211-12.degree.. XII in dry Et<sub>2</sub>O kept overnight with excess MeI and the product recrystd. gave XII.MeI, m. 170.degree. (gas evolution and formation of a resin, m. 208-9.degree.), also formed by heating 80 mg. VIII 4 hrs. in 2 ml. MeOH with 0.5 ml. MeI in excess aq. Na<sub>2</sub>CO<sub>3</sub>. In other model expts. related to work on isopavine, 14.8 g. (MeO)<sub>2</sub>CHCH<sub>2</sub>NHCH<sub>2</sub>Ph added in 3 hrs. with stirring to 20 g. 1,2-(MeO)<sub>2</sub>C<sub>6</sub>H<sub>4</sub> in 70 ml. AcOH and 70 ml. concd. H<sub>2</sub>SO<sub>4</sub>, the mixt. stirred 2 hrs., poured onto 250 g. ice, the soln. extd. twice with 250 ml. Et<sub>2</sub>O, the aq. layer basified, extd. with EtOAc, and the dried org. exts. evapd. gave a gummy product. This heated 5 hrs. at 100.degree./0.1 mm., the product (11.7 g.) taken up in 200 ml. alc., treated with 11 g. picric acid, the solid extd. with hot Me<sub>2</sub>CO from a sparingly sol. picrate (XIII) (1.27 g., m. 223-4.degree.), the Me<sub>2</sub>CO ext. evapd., the residue combined with the material obtained from evapn. of the original alc. mother liquor, the residue extd. with Me<sub>2</sub>CO, and the ext. evapd. gave 3.15 g. N-benzyl-2,2-bis(3,4-dimethoxyphenyl)ethylamine (XIV) picrate, m. 175.5-6.5.degree. (Me<sub>2</sub>CO). Recrystn. of XIII from Me<sub>2</sub>CO gave prisms, needles, and plates of 9,10-bis(benzylaminomethyl) - 9,10 - dihydro - 2,3,6,7 - tetramethoxyanthracene (XV) picrate, m. 225-6.degree. (decompn.), converted to XV, m. 156-8.degree. (alc.), which gradually changed to material softening from 130-220.degree.,  $\lambda$ . 266, 287, 350, 369 m. $\mu$ . (log  $\epsilon$ . 3.91, 3.97, 2.69, 2.68, alc.). XIV (0.71 g.) heated with HCO<sub>2</sub>H and HCHO gave 0.7 g. 2-benzyl-6,7-dimethoxy-4-(3,4-

dimethoxyphenyl)-1,2,3,4-tetrahydroisoquinoline, converted in 15 ml. Et<sub>2</sub>O by keeping 5 days with 4.5 ml. MeI to 0.8 g. product, recrystd. (MeOH) to give 0.62 g. MeI salt (XVI), m. 228-9.degree.. XVI (0.260 g.) submitted to Hofmann degradation gave 0.187 g. 1-[2-(N-benzyl-N-methylaminomethyl)-4,5-dimethoxyphenyl]-1-(3,4-dimethoxyphenyl)ethylene,  $\lambda$ . 265 m. $\mu$ . (log  $\epsilon$ . 4.17, alc.),  $\nu$ . 885, 1303, 3075 cm.<sup>-1</sup>, in keeping with the proposed structure.

IT 114162-31-1, Isoquinoline, 2-benzyl-4-(3,4-dimethoxyphenyl)-1,2,3,4-tetrahydro-6,7-dimethoxy-  
(prepn. of)

RN 114162-31-1 CAPLUS

CN Isoquinoline, 2-benzyl-4-(3,4-dimethoxyphenyl)-1,2,3,4-tetrahydro-6,7-dimethoxy- (6CI) (CA INDEX NAME)



no IA  
B  
C  
H  
Tg